In presenting the dissertation as a partial fulfillment of the requirements for an advanced degree from the Georgia Institute of Technology, I agree that the Library of the Institute shall make it available for inspection and circulation in accordance with its regulations governing materials of this type. I agree that permission to copy from, or to publish from, this dissertation may be granted by the professor under whose direction it was written, or, in his absence, by the Dean of the Graduate Division when such copying or publication is solely for scholarly purposes and does not involve potential financial gain. It is understood that any copying from, or publication of, this dissertation which involves potential financial gain will not be allowed without written permission.

7/25/68

APPROACHES TO THE SYNTHESIS OF 5/7 FUSED AND SPIROCYCLIC SESQUITERPENES

A THESIS

Presented to

The Faculty of the Graduate Division

by

James Byron Dawson

In Partial Fulfillment

of the Requirements for the Degree

Doctor of Philosophy

in the School of Chemistry

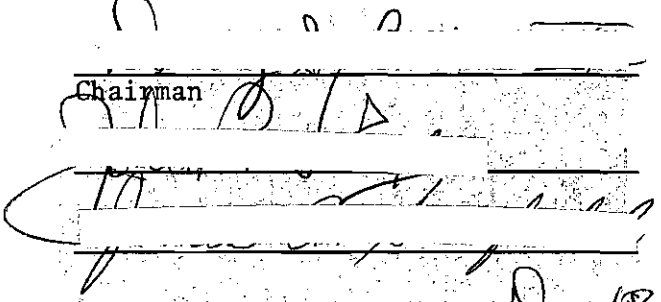
Georgia Institute of Technology

November, 1969

APPROACHES TO THE SYNTHESIS OF 5/7

FUSED AND SPIROCYCLIC SESQUITERPENES

Approved:



Chairman

Date approved by Chairman: Dec 18, 1969

ACKNOWLEDGMENTS

The author is most grateful to Dr. Drury S. Caine, III, for his valuable guidance and direction and his interest throughout the course of this work. The reading of this thesis by Dr. John R. Dyer and Dr. James A. Stanfield is greatly appreciated. The author is indebted to the U.S. Department of Health, Education, and Welfare for a National Defense Education Act, Title IV, predoctoral fellowship. The author would also like to thank Dr. John F. Debardeleben for his encouragement during the early stages of the work, Mr. George S. Turner who obtained most of the mass spectral and 100 MHz nmr data, and Mr. Richard Peveler and Mr. Tsu-i Chao for their technical assistance.

Finally, the author would like to thank his wife and family for their patience and encouragement at every step of the way.

TABLE OF CONTENTS

TABLE OF CONTENTS (CONTINUED)

TABLE OF CONTENTS (CONTINUED)

TABLE OF CONTENTS (CONTINUED)

LIST OF CHARTS

NEW COMPOUNDS

Compounds XXI, XXIII, XXVI, XXXI, XXXIII, XXIV, XXXVI, XXXVIII, XXXIX, XL, XLI, XLII, XLIII, XLIV, XLV, XLVI, XLVIII, XLIX, L, LI, LII, LIII, LIV, LVI, LVII, and LXIV are new compounds prepared during the course of this work. Structures for these compounds will be found in the appendix.

GLOSSARY OF ABBREVIATIONS

DDHQ	2,3-dicyano-5,6-dichlorobenzohydroquinone
DDQ	2,3-dicyano-5,6-dichlorobenzoquinone
DME	1,2-dimethoxyethane
glc	Gas Liquid Chromatography
Hz	Hertz
nm	Nanometer
nmr	Nuclear Magnetic Resonance
ppm	Parts per million
SE-30	Silicone Gum Rubber(methyl)
tlc	Thin Layer Chromatography
THF	Tetrahydrofuran
TMS	Tetramethysilane

SUMMARY

There were two primary goals of this research. The first was to investigate further the photochemical rearrangement of cross-conjugated cyclohexadienones with electron withdrawing substituents on the dienone chromophore. The second was to attempt to apply such photochemical rearrangements to the synthesis of natural products whose basic ring skeletons are related to the ring skeletons of the products obtained on irradiation of cyclohexadienones.

Attempts were made to prepare three new dienones with electron withdrawing substituents at the four position. The enone, 3-keto-4-carbomethoxy-9-methyl-Δ^{4}-octahydronaphathalene (I) was prepared according to known methods. All attempts at converting I to the corresponding dienone, 3-keto-4-carbomethoxy-9-methyl-$\Delta^{1,4}$-hexahydronaphthalene (II) were unsuccessful. The enone, 3-keto-4-formyl-9-methyl-Δ^{1}-octahydronaphthalene (III) was prepared according to a known procedure. This compound was converted into 3-keto-4-formyl-9-methyl-$\Delta^{1,4}$-hexahydronaphthalene (IV) in 53 percent yield. Compound III was also converted into 3-keto-4-cyano-9-methyl-Δ^{1}-octahydronaphthalene (V) by a known procedure in 50 percent yield. Compound V was converted into 3-keto-4-cyano-9-methyl-$\Delta^{1,4}$-hexahydronaphthalene (VI) according to a known method in 86 percent yield.

Irradiation of compound IV was carried out in aqueous acetic acid. Indications were that between IV and 3-keto-4-formyl-9-methyl-$\Delta^{1,6}$-hexahydronaphthalene (VII) an equilibrium was set up which was probably

thermal and not photochemical. Irradiation of VI gave a 24 percent yield of 3-keto-4-cyano-6β-methyl-6α-hydroxy-(4.5)spirodecene-1 (VIII), a 3 percent yield of 1-methyl-2-cyano-3-hydroxy-5,6,7,8-tetrahydronaphthalene and a 13 percent yield of a compound tentatively identified as 2-keto-3-cyano-8β-methyl-4,5,6,7,8aβ-hexahydro-8α-hydroxy-2(1H)-azulenone (X). The suggested structures of VIII, IX, and X were supported by their physical properties and comparison of these properties with known properties of similar compounds.

In accordance with an attempt to synthesize the originally proposed structure of β-vetivone, 2-carboxy-3-keto-5α,9-dimethyl-7-ethylenedioxy-$\Delta^{1,4}$-hexahydronaphthalene (XI) was prepared and irradiated in aqueous acetic acid. A 17 percent yield of 1β-carboxy-4α,8β-dimethyl-6-ethylenedioxy-4,5,6,8aα-hexahydro-8α-hydroxy-2(1H)-azuleneone lactone (XII) and a 35 percent yield of 4α,8β-dimethyl-6-ethylenedioxy-4,5,6,-7,8aα-hexahydro-8α-hydroxy-2(1H)-azulenone (XIII) were obtained. The suggested structures of these compounds were supported by their physical properties and by comparison of these properties with those of similar known compounds.

Two compounds, 2-methoxy-3-keto-9-methyl-$\Delta^{1,4}$-hexahydronaphthalene (XV) and its 5α-methyl isomer (XVI) were synthesized in connection with the proposed synthesis of the naturally occurring sesquiterpene alcohols, hinesol and agarospirol. They were prepared from 3-keto-9-methyl-Δ^{4}-octahydronaphthalene (XVI) and 3-keto-5aα,9-dimethyl-Δ^{4}-octahydronaphthalene (XVII) respectively in approximately 25 percent yield using a combination of known methods. Irradiation of these compounds gave an approximately 30 percent yield of the expected spirohydroxy ke-

tones, XVIIIand XIX, respectively. The suggested structures of these compounds were supported by their physical properties and by comparison of these properties with those of similar known compounds.

Compound XIX, 2-methoxy-3-keto-6α,10α-dimethyl-6β-hydroxyspiro-(4.5)decene-1, was converted into compound XX, 3-keto-6,10α-dimethyl-spiro(4.5)decene-6 by a series of reactions including dehydration, reduction, acetylation, reduction, and hydrolysis. Each of these reactions required extensive study before the desired results were achieved.

Attempts were made to convert XX into hinesol and agarospirol by first preparing the acetylenic carbinol XXI corresponding to the addition of acetylene across the carbonyl of XX. Compound XXI on dehydration followed by hydration of the triple bond would have given rise to a methyl ketone, XXII, which had previously been converted into the natural products mentioned. This series of reactions was not successful; however, attempted hydrolysis of a material thought to be XXI gave a compound identical to the octalone XVII. Subsequent treatment of XX in the same manner also gave a compound identical to known XVII.

CHAPTER I

INTRODUCTION

In the past few years there has been an active interest in the photochemical rearrangements of cross-conjugated cyclohexadienones of the type I. The first known rearrangement of such a compound was reported in connection with work on α-santonin, II* in 1830 (1). It has since been well documented (2) that rearrangements of cross-conjugated cyclohexadienes in aqueous acetic media produce varying yields of hydroxy ketones of the types III and IV, (see chart I) and, furthermore the relative yields of the two hydroxy ketones are influenced significantly by the electronic nature of substituents on the cyclohexadienone chromophore. The exact mechanistic details of the rearrangement have not been determined; however, the intermediacy of mesoionic species is widely accepted. Several systems of notation for illustrating the pathways by which these hypothetical zwitterions might arise have appeared in the literature (3,4,5). The notation suggested by Zimmerman is shown in Chart 1. In the first step (equation 1), I undergoes an $n \rightarrow \pi^*$ electronic excitation to give the resonance stabilized diradical V. The species V then undergoes 1,5 bonding to give the excited state cyclopropyl intermediate VI as shown in equation 2. The cyclopropyl intermediate then undergoes a $\pi^* \rightarrow n$ demotion to the zwitterionic species VII. At this point the character of the solvent becomes important. If an inert sol-

*Structural formula of all compounds discussed may be found in the Appendix.

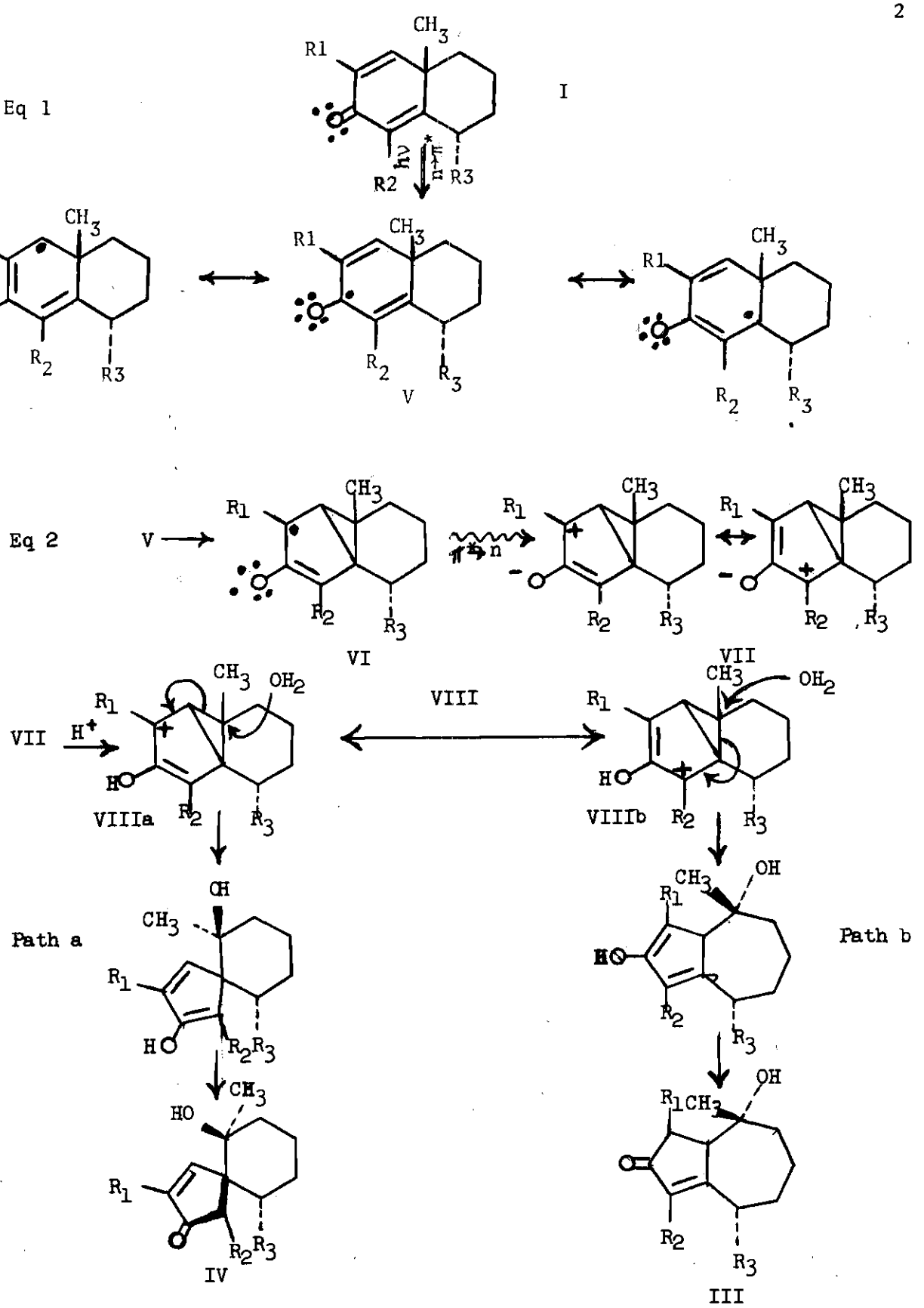


Chart 1. Mechanism of Photochemical Rearrangements of Cross-Conjugated Cyclohexadieneones

a $R_1 = R_2 = H$, $R_3 = CH_3$

b $R_1 = CH_3$, $R_2 = R_3 = H$

c $R_1 = R_3 = H$, $R_2 = CH_3$

d $R_1 = CO_2H$, $R_2 = R_3 = H$

e $R_1 = CO_2CH_3$, $R_2 = R_3 = H$

f $R_1 = CHO$, $R_2 = R_3 = H$

g $R_1 = R_2 = R_3 = H$

Chart 1. (Continued)

vent is used, VII rearranges to a tricyclic ketone called a lumi product (1), however if a protic solvent is used, VII yields the mesomeric cation VIII. Cleavage of VIII via path A gives the enolic form of the spiro hydroxy ketone IV, while cleavage of VIII via path B gives the enolic form of the 5/7 fused hydroxy ketone III. In either case spontaneous ketonization gives rise to the products, III and IV. In most of the cases reported, the solvent is aqueous acetic acid and the attacking nucleophile is water. However, rearrangements can be carried out in glacial acetic acid where the nucleophile involved is acetic acid.

With respect to the influence of substituents at C-1 and C-3 of the chromophore, it is obvious from inspection of the resonance hybrid VIII that factors which would lead to stabilization of positive character at C-1 or C-3 should favor VIIIA or VIIIB, respectively. In light of this observation it follows that a substituent at C-1 of VIIIA with electron releasing character should direct the rearrangement toward a predominance of VIIIA and lead to the spiro compound IV, while an analogous situation at C-3 of VIII should direct the rearrangement through VIIIB toward a predominance of the 5/7-fused ketone III. This expected influence has been observed in a number of cases. Irradiation of Ia (6) in 45 percent aqueous acetic acid gave 19 percent of IIIa and 16 percent of IVa. A similar irradiation of Ib (7) gave a 51 percent yield of IVb, while Ic (8) gave an 80 percent yield of IIIc. These findings support completely the intervention of an intermediate of the type VIII in rearrangements of unsubstituted methylated dienones. Further support for this mechanism is found in studies on the effects of electron withdrawing substituents on the rearrangement. In these cases one expects to observe, for a given

substitution pattern, an opposite effect from that found with electron donating substituents. Indeed, irradiation of Id (9) in aqueous acetic acid gives a 60 percent yield of IIIg after spontaneous decarboxylation, and irradiation of Ie (10) gives a 67 percent yield of IIIe. Irradiation of If (11) in the same manner followed by treatment of the crude photo product with aqueous sodium carbonate gives a 70 percent yield of compound IX. These findings are again in complete agreement with the existence of an intermediate of the type represented by VIII.

It would seem, from the facts presented, that such rearrangements of cyclodienones should be readily applicable to synthetic sequences directed toward the preparation of certain naturally occurring compounds whose basic ring skeletons are of the 5/7-fused or (4.5)-spiro type.

There are a variety of naturally occurring sesquiterpenoids having ring skeletons based on azulene (12a,b,c). Most of the hydroazulenes are derivatives of guaiane including geigerin (X) (13), and the bicyclic alcohols guaiol (XI) (14) and bulnesol (XII) (14). Other hydroazulene types are represented by the tricyclic ketone cyclocolorenone (XIII) (15a,b), and the hydrocarbons aromadendrene (XIV) (16) and α-gurjuene (XV) (17). It was once thought that the sesquiterpenes α-vetivone (XXV), β-vetivone (XVI) (18) and hinesol (XVII) (19) were also of the perhydroazulene family but XVI and XVII have recently been shown to be of the (4.5) spiro skeleton by Marshall (20) while XXV is a member of the eremophalone family according to de Mayo (21). Along with XVI and XVII, there is another naturally occurring spirocyclic alcohol, agarospirol (XVIII) (22), which is of interest.

The purpose of the work to be discussed in this thesis was to investigate further the effect of electron withdrawing substituents on the photochemical rearrangements of cross-conjugated cyclohexadienones and to attempt to apply the rearrangement to the synthesis of natural products having basic ring systems accessible through the rearrangement. The initial decision was to synthesize β-vetivone whose structure was originally reported to be XIX (18). It was felt that irradiation of a derivative of Id substituted in the appropriate manner would lead to the required A ring unsubstituted hydroazulene. Such a compound had been prepared by DeBardeleben (10) and the results of the rearrangement of this compound are reported. During the course of this initial work it was reported that the structure of β-vetivone was incorrect and should be revised to XVI (20). In view of this fact it became obvious that the structure of hinesol, which had been correlated with β-vetivone (23), could not be of the hydroazulene type but must also be of the (4.5)-spiro decane type. Furthermore, since agarospirol was of the structure indicated by XVIII it was necessary that hinesol and agarospirol be identical to each other with the exception of the stereochemistry about C-2, the point of attachment of the three carbon side chain in XVIII. It thus became necessary to find a method of preparing ring-A unsubstituted spirodecanes in yields suitable for synthetic requirements. Also, since the stereochemistry of the spirodecanes obtained from photochemical rearrangement was opposite to that needed for synthesis of any of the natural products mentioned, it was necessary to devise a method that would both direct the rearrangement toward A-ring unsubstituted compounds

and allow for the necessary change in stereochemistry. The two alcohols, hinesol and agarospirol, were chosen for synthesis. Since hinesol had previously been converted to β-vetivone the synthesis of this compound would also effect a total formal synthesis of β-vetivone. The remainder of the work was then centered around selecting a suitable dienone, preparing this dienone, and converting the rearrangement product of this dieneone into the sesquiterpenes mentioned above.

CHAPTER II

INSTRUMENTATION AND EQUIPMENT

Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. Boiling points are uncorrected. Carbon and hydrogen microanalyses were performed by Galbraith Laboratories, Knoxville, Tennessee. Mass spectral data were acquired using a Varian Associates Model M-66 medium resolution mass spectrometer. All exact mass determinations reported agree to within 0.005 of the calculated value and were verified as being the only reasonable possibilities with the aid of "Chemical Formulae From Mass Determination" (24). Ultraviolet spectra were recorded on a Cary Model 14 recording spectrophotometer using one centimeter balanced cells with 95 percent ethanol as the solvent. Infrared spectra were obtained on a Perkin-Elmer Model 137, 237, or 457 recording spectrophotometer using 0.2 mm sodium chloride cells with chloroform as the solvent unless otherwise specified. Nuclear magnetic resonance spectra were obtained on a Varian Associates Model A-60 or A-60D, nuclear magnetic resonance spectrometer, or on a Jeolco Model 4H-100 nuclear magnetic resonance spectrometer. Unless otherwise noted, carbon tetrachloride containing tetramethyl silane as an internal standard was used as solvent. Chemical shifts are reported in ppm downfield from the standard. The abbreviations s, d, t, q, and m, refer respectively to singlet, doublet, triplet, quartet, and multiplet; coupling constants (J) are given in Hz. Hydrogenations were carried out

in a Parr low pressure reaction apparatus using 95 percent ethanol as solvent. Low pressure solvent evaporations were accomplished with the aid of a Büchi Rotavapor rotary evaporator. Gas chromatographic analyses were performed on either a Perkin-Elmer Model 881 flame ionization gas chromatograph programmed from 50° to 225°C at 12 degrees per minute using a 6 foot by 1/8 in. column packed with 10 percent Apeizon L on 60/80 Chromosorb W, or a Hewlett-Packard Model 402 flame ionization gas chromatograph programmed from 60° to 240°C at 15 degrees per minute using a 4 foot by 3 mm column packed with 3.8 percent SE-30 on 80/100 Diatoport S. Preparative gas chromatography was accomplished with the aid of a Hewlett-Packard Model 700 gas chromatograph equipped with a thermal conductivity detector. A 3 foot by 1/4 in. stainless steel column packed with silicone rubber on 80/100 Diatoport S at 200° was used for preparative work. Grace grade 923, 100-200 mesh silica-gel was used for column chromatography unless otherwise specified. Anhydrous sodium sulfate was used as drying agent in reaction workups. Reagent grade inorganic chemicals were used throughout, while liquid organic chemicals were distilled prior to use. Anhydrous solvents were prepared by distillation from sodium or lithium aluminum hydride with the exception of anhydrous ether which was purchased commercially and stored over sodium ribbon. A Hanovia 450 watt high pressure mercury lamp or a Hanau NK20 7 watt low pressure source having greater than 90 percent of its output at 2537 Angstroms were used for photochemical irradiations. An apparatus similar to that described by Kropp and Erman (6) was used for the high pressure source while a simple immersion tank was used for the 7 watt source. During irradiations the solutions were agitated by

a stream of nitrogen introduced at an appropriate point. An inert atmosphere of nitrogen was maintained over reaction mixtures when necessary by an apparatus similar to that described by Johnson (25). Recrystallizations from mixed solvents were carried out by dissolving the material to be recrystallized in the minimum amount of the more polar solvent, adding the second solvent dropwise until the solution became cloudy, warming on the steam bath until the solution became clear, and allowing crystallization to take place as the solution cooled. Thin layer chromatography was carried out using glass plates coated with silica gel.

CHAPTER III

EXPERIMENTAL

Irradiation of 2-Carboxy-3-keto-5,9-dimethyl-7-ethylenedioxy -$\Delta^{1,4}$hexahydronaphthalene (XX)

Compound XX (0.80 g) prepared according to the method of DeBardeleben (10) was dissolved in 250 ml of 45 percent aqueous dioxane and irradiated with a 450 watt high pressure mercury lamp for 1.75 hrs. using a Pyrex filter. Benzene was added and the solvent was removed in vacuo with the aid of a benzene azeotrope to leave a dark brown viscous oil. The crude reaction product was chromatographed over 20 g of silica gel. Elution successively with 500 ml of hexane, 500 ml of 10 percent ether in hexane, 1000 ml of 20 percent ether in hexane, and 250 ml of 50 percent ether in hexane gave on evaporation, four oily residues, which were shown to be complicated mixtures of compounds by tlc. Further elution with 250 ml of 50 percent ether in hexane followed by 500 ml of 75 percent ether in hexane gave 0.139 g (17 percent) of a yellow oil which crystallized on standing. Recrystallization from ethyl acetate-hexane gave white crystals melting at 192-194^{o}C with decomposition. The material was identified as 1β-carboxy-4α,8β- dimethyl-6-ethylenedioxy-4,5,6,7,8α-hexahydro-8α-hydroxy-2(1H)-azulenone lactone (XXI) by its spectral properties listed below and by spectral analogy with the known azulenone lactone (XXII) (10). The infrared spectrum of XXI showed, among others, absorptions at $\nu_{max}^{CHCl_3}$ 1787 (α-lactone carbonyl), 1710

α,β-unsaturated cyclopentanone), and 1591 cm^{-1}(conjugated double bond). The ultraviolet spectrum showed λ_{max}^{EtOH} 244 nm (ε 13,900). The nmr spectrum of II showed $\delta_{TMS}^{CDCl_3}$ 1.21 (s, 3H, 8β-CH_3), 1.14 (d, J=6Hz, 4α-CH_3, 3.94) (s, 4H, -OCH_2-), and 5.89 (m, 1H). Exact mass: Calculated: 278.1154, Found: 278.1144.

Further elution with 1250 ml of 100 percent ether and 1000 ml of methanol gave 0.683 g of a mixture of compounds. This material was rechromatographed on 20 g of neutral alumina, activity I. Elution with 500 ml of 75 percent ether in hexane, 500 ml of 90 percent ether in hexane, and 250 ml of 100 percent ether gave three mixtures of unidentified products. Finally elution with 500 ml of 10 percent methanol in ether, and 250 ml of 15 percent methanol in ether gave 0.297 g (35 percent) of a pale yellow solid. Recrystallization from ether gave white crystals melting at 141-142°C. The material was identified as 4α,8β-dimethyl-6-ethylenedioxy-4,5,6,7,8aα-hexahydro-8β-hydroxy-2(1H)-azuleneone XXIII by spectral analogy with the known azulenone XXIV (10) and by its spectral properties described below. The infrared spectrum of XXIII showed, among others, absorptions at $\nu_{max}^{CHCl_3}$ 3450(hydroxyl), 1680 (α,β-unsaturated cyclopentanone), and 1590 cm^{-1} (conjugated double bond). The ultraviolet spectrum showed a λ_{max}^{ETOH} 234 nm (ε10,300). The nmr spectrum of XXIII showed the following absorptions: $\delta_{TMS}^{CDCl_3}$ 1.05 (s, 3H, 8β-CH_3), 1.21 (d, J-7 Hz, 3H, 4α-CH_3), 3.98 (s, 4H, -OCH_2-), and 6.03 (m, 1H). Analytical: Calculated: C 66.64, H 7.99, Found: C 66.42, H 8.02.

Isolation of α- and β-Vetivones from Oil of Vetiver

Two procedures for the isolation of α- and β-vetivones, spinning band column distillation followed by preparative glc collection or, isolation of the ketonic portion of the oil with Girard's T reagent followed by preparative glc, were attempted. The more satisfactory of the two is described below.

Oil of Vetiver(Reunion)* (40 g), 8 g of Girard's T reagent, and 15 ml of glacial acetic acid were dissolved in 200 ml of 95 percent alcohol and heated at reflux for two hours. Following removal of approximately 175 ml of the alcohol by distillation, 100 ml of water was added. The reaction mixture was washed thoroughly with ether. The remaining aqueous solution was then acidified with 10 ml of concentrated hydrochloric acid and heated for 20 min. on the steam bath. After being cooled to room temperature the reaction mixture was extracted thoroughly with ether. The ether extracts were dried over anhydrous sodium sulfate, the drying agent was removed by filtration, and the ether was removed under reduced pressure to leave a viscous yellow oil. The oil was distilled at 110-125°C at 0.5 mm and the resulting material subjected to preparative glc at 205°C using a three foot by 1/4 in. metal column packed with Apeizon L on 60/80 firebrick. The infrared spectrum of α- and β-vetivones were identical to those reported by Nigam (28). The nmr spectra were as follows: For α vetivone XXV $\delta^{CCl_4}_{TMS}$ 0.95 (s, 3H, angular CH_3), 1.0 (d, J=6Hz, 3H, 1-CH_3), 1.71 (s, 6H, isopropylidene-CH_3),

---

*The author would like to thank Fritzche Bros. Inc. for their generosity in supplying the oil of Vetiver.

and 5.65 (m, 1H). For β-vetivone XVI $\delta^{CCl_4}_{TMS}$ 0.91 (d, J=7 Hz, 3H, 4-CH_3), 1.61 and 1.67 (s, 3H, isopropylidene-CH_3), 1.84 (d, J=1.2, 3H, vinyl CH_3), and 5.65 (m, 1H).

Preparation of 4-Carbomethoxy-3-keto-9-methyl-Δ^4-octahydronaphthalene (XXVI)

A procedure similar to that employed by Wenkert (27) in another system was used. To a suspension of 1.12 g (0.025 moles) of 53.4 percent sodium hydride-mineral oil dispersion in 50 ml of dry DME stirred under nitrogen was added 5 g (0.03 moles) of 3-keto-9-methyl-Δ^4-octahydronaphthalene (XXVII) (28a). The solution was stirred at room temperature overnight, heated to reflux, and the solvent removed by distillation until the volume remaining was approximately 20 ml. The reaction mixture was allowed to cool to room temperature and 100 ml of dry ether was added. Carbon dioxide which had been passed through a calcium chloride drying tube was then allowed to bubble into the solution for 1.25 hrs while the temperature was maintained at 0°C by an ice bath. At the end of this time 50 ml of 10 percent sodium hydroxide was added to the cold reaction mixture and stirring was continued for an additional 15 min. The basic solution was then washed with three 50 ml portions of ether and acidified to pH 2-3 with dilute (3:1) hydrochloric acid at which time the solution became cloudy. The aqueous layer was then extracted with ether and the ether extracts were poured slowly into a stirred solution of diazomethane in ether (28b). The cold reaction mixture was stirred for 0.5 hrs after which the excess diazomethane was destroyed with aqueous hydrochloric acid. The layers were separated and the organic layer was washed twice with 50 ml portions of saturated sodium bicarbonate solution and once with saturated brine. The solution

was then dried over anhydrous sodium sulfate, the drying agent removed by filtration, and the solvent removed in vacuo to leave 3.71 g (55 percent) of XXVI as a pale yellow oil. Thin layer chromatography showed the material to be essentially one compound. The infrared spectrum of XXVI showed, among others, absorptions at $\nu_{Max}^{CHCl_3}$ 1730 (ester carbonyl), 1668 (α,β unsaturated ketone), and 1605 cm^{-1} conjugated double bond). The nmr spectrum of XXVI showed $\delta_{TMS}^{CCl_4}$ 1.29 (s, 3H, 9-CH_3) and 3.69 (s, 3H, -CO_2CH_3).

Attempted Preparation of 4-Carbomethoxy-3-keto-9-methyl-$\Delta^{1,4}$-hexahydronaphthalene (XXVIII)

The general procedure of Burn et al. (29) was employed. In a typical experiment a solution of 1.58 g (0.0071 moles) of XXVI in 75 ml of dry dioxane stirred under nitrogen was treated with 2.01 g of DDQ. The total volume was brought to 100 ml with additional dioxane and the reaction mixture was heated at reflux for 48 hr. The mixture was evaporated to near dryness and the precipitated DDHQ was removed by filtration. The remaining solvent was removed in vacuo to leave a dark brown oil. The previous experiment was repeated under the conditions listed below:

Solvent	Reflux Time	Method of DDHQ Removal
Dioxane	22 hours	Filtration through alumina
Benzene	17 hours	Suction filtration
Dioxane	12 hours	Filtration followed by washing with 10 percent sodium hydroxide
Toluene/HOAc	20 hours	Filtration followed by washing with 10 percent sodium hydroxide

In each case after solvent removal both column chromatography and distillation were tried separately and in combination as a means of further purifying the products, but all attempts failed to separate the mixture of compounds. The spectral characteristics of the mixture indicated it was composed of compounds of the type XXVIII, XXIX, and XXX.

Preparation of 3-Keto-4-formyl-9-methyl-Δ^1-octahydronaphthalene (XXXI)

The general method of Woodward et al. (30) was employed. To a suspension of 3.85 g (0.160 moles) of sodium hydride stirred in 100 ml of dry benzene under nitrogen was added dropwise 3.46 g (0.108 moles) of anhydrous methanol. The suspension was heated to reflux for a few minutes, cooled to room temperature, and 11.8 g (0.160 moles) of freshly distilled ethyl formate was added in a thin stream. The reaction mixture was then stirred for 0.5 hr, cooled to 0°C in an ice bath, and 10.5 g (0.064 moles) of 3-keto-9-methyl-Δ^1-octahydronaphthalene (XXXII) (31) dissolved in 150 ml of dry benzene was added dropwise with stirring and cooling. Shortly after the addition was begun a yellow precipitate formed. After the addition was complete, the cooling bath was removed

and the suspension was allowed to stir overnight. The yellow suspension was then acidified with 100 ml of iced 5 percent sulfuric acid and allowed to stir for 5 min. The layers were separated, and the aqueous layer was extracted with 1:1 ether-benzene. The combined organic layers were washed with 4 X 50 ml portions of 2 percent potassium hydroxide, the basic extract was washed once with ether and then acidified with dilute hydrochloric acid. The acidified aqueous layer was then extracted thoroughly with several portions of 1:1 ether-benzene. The organic extracts were washed with saturated brine and dried over anhydrous sodium sulfate. After removal of the drying agent the volatile solvents were removed in vacuo to leave a viscous yellow oil whose properties were found to be as follows. The ultraviolet spectrum showed λ_{Max}^{EtOH} 244 nm (4900) 305 nm (ε 3900), $\lambda_{Max}^{EtOH+NaOH}$ 237 nm, ε 8750, 324 nm, ε 4950. The infrared spectrum showed, among others, absorptions at $\nu_{Max}^{CHCl_3}$ 1645 (α,β unsaturated ketone), and 1565 cm^{-1} (conjugated double bond). The nmr spectrum showed absorptions at $\delta_{TMS}^{CCl_4}$ 0.86 (s, 3H, 9-CH_3), 2.4 (d broad, J=9 Hz, 1H, 6-H), 5.75 and 6.58 (AB quartet, J_{AB} = 10 Hz, 2H, 1,2-H), 7.09 (d, J=10 Hz, 0.9 H, =C-H), 8.5 (s, 0.1 H, =CHO), and 13.9 (d, J=10 Hz, 0.9 H, =C-OH. Exact Mass: Calculated: 192.1150, Found: 192.1048. The material weighed 6.5 g (53 percent).

Preparation of 3-Keto-4-formyl-9-methyl-$\Delta^{1,4}$-hexahydronaphthalene (XXXIII)

The general method of DeBardeleben was employed (10). To a solution of 3.54 g (0.018 moles) of XXXI dissolved in 100 ml of anhydrous dioxane was added 4.52 g (0.02 moles) of DDQ dissolved in 100 ml of anhydrous dioxane. The solution was swirled for four minutes, poured into

300 ml of methylene chloride and filtered with pressure through a column of silica gel. The column was then eluted with 300 ml more of methylene chloride. The eluent was a cloudy green at this point therefore it was stirred with 5 g of Norit on the steam bath for a few minutes and filtered through Celite. Evaporation of the resulting yellow solution gave an oily solid. The solid portion was soluble in sodium bicarbonate; therefore the crude reaction product was dissolved in ether and this solution washed with sodium bicarbonate solution and then with saturated brine. The ethereal solution was then dried over anhydrous sodium sulfate, the drying agent removed by filtration and the solvent removed in vacuo to leave 2.24 g (64 percent) of XXXIII whose properties are listed below. The infrared spectrum of XXXIII showed, among others, absorptions at $\lambda_{Max}^{CHCl_3}$ 1667 (α,β unsaturated ketone), and 1625 cm^{-1} (conjugated double bond). The ultraviolet spectrum showed λ_{Max}^{EtOH} 242 nm (ε12,000). The nmr spectrum showed absorptions at $\delta_{TMS}^{CCl_4}$ 1.39 (s, 3H, 9-CH_3), 3.80 (d-broad, J=14 Hz, 1H, 6H), and 6.17 and 6.81 (AB quartet, J_{AB}=10 Hz, 2H, 1,2-H). Exact Mass: Calculated: 190.0990, Found: 190.0954.

Irradiation of 3-Keto-4-formyl-9-methyl-$\Delta^{1,4}$-hexahydronaphthalene (XXXIII)

Compound XXXIII (2.24 g) was dissolved in 250 ml of 45 percent aqueous acetic acid and irradiated with the 450 watt source employing a Pyrex filter for 1.5 hr. Benzene was added and the solvent removed in vacuo with the aid of a benzene azeotrope until the odor of acetic acid was gone, leaving a viscous oil. The nmr spectrum of the crude reaction mixture showed as the only significant absorptions, in addition to the absorptions of the starting material, $\delta_{TMS}^{CCl_4}$ 6.07 and 6.74 (AB quartet,

J_{AB}=10 Hz), 5.32 (s, broad), and 1.36 (s). Further qualitative (ir) examination showed the material to be mainly unreacted starting material (XXXIII). Vacuum distillation of the reaction mixture gave a reddish-yellow oil boiling at 105-115/0.1 mm. The nmr spectrum of this material showed absorptions identical to those described above, but in a vastly different ratio of peak areas. (4:1 for the crude reaction product as compared to 1:1.6 for the distilled material.) This ratio was noted to change slightly in the direction of the photo product on standing overnight at room temperature.

Further irradiation of this material for 2.5 hr with a 2537 Å source in 45 percent aqueous acetic acid followed by the usual workup gave a material whose nmr spectrum was identical to that of XXXIII. In addition, irradiation of XXXIII for 4 hours with the 2537 Å source in anhydrous dioxane gave, after removal of the solvent in vacuo a polymeric mass with no well defined spectral characteristics. Qualitative analysis by glc showed the mass to consist of a large number of compounds.

Preparation of 3-Keto-4-cyano-9-methyl-Δ^1-octahydronaphthalene (XXXIV)

The procedure of Kuehene (32) was followed for the preparation of XXXIV. Compound XXXII, 6.5 g (0.034 moles) was dissolved in 250 ml of glacial acetic acid along with 4 g of hydroxylamine hydrochloride. The solution was heated at reflux in a nitrogen atmosphere for two hours, after which the solvent was almost completely removed by distillation at aspirator pressure. The residue was allowed to cool, dissolved in chloroform (100 ml) and washed twice with 25 ml of sodium hydroxide solution, followed by washing with water. The solution was dried with

anhydrous sodium sulfate, the drying agent removed by filtration, and the solvent removed in vacuo to leave the isoxazole XXXV. Compound XXXV was not further purified but was stirred for 0.75 hr at room temperature under nitrogen with a suspension prepared from 30 ml of anhydrous methanol, 1.32 g of sodium metal, and 300 ml of anhydrous benzene. The reaction mixture was then extracted several times with 50 ml portions of 0.5 percent potassium hydroxide solution. The basic extracts were acidified with dilute hydrochloric acid and the acidified aqueous solution was extracted thoroughly with chloroform. The chloroform solution was washed with water, dried over sodium sulfate, and the drying agent removed by filtration. The solvent was removed in vacuo to leave a pale yellow oil which solidified on standing to give 3.2 g (50 percent) of XXXIV. Recrystallization from ether-hexane gave white crystals melting at 70.5-71.5°C (softening at 65°C). The ultraviolet spectrum of XXXIV showed λ_{Max}^{EtOH} 227 nm, ε 7800. The infrared spectrum of XXXIV showed among others, absorptions at $\nu_{Max}^{CHCl_3}$ 2247 (-CN), 1681 (α,β unsaturated ketone), and and 1613 cm^{-1} (conjugated double bond). The nmr spectrum of XXXIV showed $\delta_{TMS}^{CCl_4}$ 1.11 (s, 3H, 9-CH_3), 3.40 (d, J=13 Hz, 1H, 4-H), and 5.80 and 6.81 (AB quartet, J_{AB}=10 Hz, 2H, 1-2H). Exact Mass: Calculated: 189.1154, Found: 189.1150.

Preparation of 3-Keto-4-cyano-9-methyl-$\Delta^{1,4}$-hexahydronaphthalene (XXXVI)

The method of Kissman (33) was employed for the synthesis of XXXVI. To a solution of 4.4 g (0.02 moles) of DDQ dissolved in 100 ml of dry dioxane was added 2.5 g (0.13 moles) of XXXIV dissolved in 50 ml of

dry dioxane. The solution was heated to reflux with stirring overnight. The reaction mixture was allowed to cool to room temperature, and the solvent was removed in vacuo. The residue was dissolved in 50 ml of benzene and filtered to remove the bulk of the DDHQ. The benzene solution was first washed with 0.5 percent sodium hydroxide solution then with saturated brine and finally dried over anhydrous sodium sulfate. The drying agent was removed by filtration, and the solvent was evaporated in vacuo to give 2.1 g (86 percent) of a pale yellow oily solid. Recrystallization from ether-hexane gave white needles melting at 78.5-79°. The ultraviolet spectrum showed λ_{MAX}^{EtOH} 247 nm, ε 17,300. The infrared spectrum of XXXVI showed, among others, absorptions at $\nu_{Max}^{CHCl_3}$ 2235 (-CN), 1662 (α,β unsaturated ketone), and 1591 cm^{-1} (conjugated double bond). The nmr spectrum of XXXVI showed absorptions at $\delta_{TMS}^{CCl_4}$ 1.4 (s, 3H, 9-CH_3), 2.87 (t-broad, 1H, 6-H), 6.19 and 6.94 (AB quartet, J_{AB} = 10 Hz, 2H, 1, 2H). Analytical: Calculated: C 76.97, H 6.99, Found: C 77.20, H 7.06.

Irradiation of 3-Keto-4-cyano-9-methyl-$\Delta^{1,4}$-hexahydronaphthalene (XXXVI)

A solution of 2.1 g (0.01 moles) of XXXVI dissolved in 250 ml of 45 percent aqueous acetic acid, was irradiated for 4.5 hr with the 450 watt source using a Pyrex filter. Benzene was added and the solvent removed in vacuo with the aid of a benzene azeotrope until the odor of acetic acid was gone to yield 1.22 g of a viscous brown oil. The crude product was chromatographed over 40 g of silica gel. Elution with 150 ml each of 15, 20, and 25 percent ether in hexane gave a total of 0.61 g (3 percent) of a white solid melting, after recrystallization from

ether, at 179-180°C which was base soluble and gave a positive ferric chloride test according to Soloway (34). The ultraviolet spectrum showed λ_{Max}^{EtOH} 246 nm (ε 9870), 250 nm (ε 953), λ_{Min}^{EtOH} 300 nm, ε 3610, 304 nm, ε 3800. The infrared spectrum showed, among others, absorptions at $\nu_{Max}^{CHCl_3}$ 3550 (-OH), 2215 (-CN), 1615 and 1565 cm^{-1}. The nmr spectrum of the compound exhibited absorptions at $\delta_{TMS}^{CDCl_3}$ 2.39 (s, 3H, Ar-CH_3), and 6.57 (s, 1H, Ar-H). Exact Mass: Calculated: 187.0994, Found: 187.0966. On the basis of the above data and comparison with the known phenol XXXVII (6), the compound was assigned the structure XXXVIII. Further elution with 150 ml each of 30, 35, 40, and 45 percent ether in hexane gave a total of 0.302 g (13.5 percent) of a viscous yellow oil whose spectral properties exhibited the following characteristics. The ultraviolet spectrum showed λ_{Max}^{EtOH} 238 nm (ε 8800). The infrared spectrum showed, among others, absorptions at $\nu_{Max}^{CHCl_3}$ 2235 (-CN), 1690 (α,β unsaturated cyclopentanone), and 1605 cm^{-1} (conjugated double bond). The nmr spectrum showed significant absorptions at $\delta_{TMS}^{CDCl_3}$ 1.15 (s, 3H, tert.-CH_3). No absorption in the region 4.0 - 7.0 ppm was observed. Although mass spectral analysis failed to show the desired molecular ion (m/e 205) the compound was assigned the structure XXXIV on the basis of the above data and in analogy to the known perhydroazulene III_c (8). Continued elution with 150 ml each of 55, 60, and 65 percent ether in hexane gave a total of 0.372 g of a mixture of two compounds the major component of which was identified as starting material. Finally elution with 150 ml each of 70, 75, 80, 85, 90, 95 ether in hexane gave a total of 0.488 g (24 percent) of a viscous yellow oil

which showed the following properties. The ultraviolet spectrum showed λ_{Max}^{EtOH} 227 nm, ε 6500. The infrared spectrum showed, among others, absorptions at $\nu_{Max}^{CHCl_3}$ 3590 (-OH), 2245 (-CN), 1722 (α,β unsaturated cyclopentanone), and 1602 cm^{-1} (conjugated double bond). The nmr spectrum showed absorptions at $\delta_{TMS}^{CDCl_3}$ 1.35 (s, 3H, tert.-CH_3), 3.87 (s, 1H, 4-H), and 6.20 and 8.11 (AB quartet, J_{AB}=5.5 Hz, 2H, 1,2-H). Exact Mass: Calculated: 205.1102, Found: 205.1102. On the basis of the above data and in analogy to the known spiro ketone IV_g (6), the compound was assigned to the structure XL.

Preparation of 2-Acetoxy-3-keto-9-methyl-Δ^4-octahydronaphthalene (XLI)

The method of Seeback (35) was employed for the synthesis of XLI. To a solution of 41 g (0.093 moles) of lead tetraacetate dissolved in 200 ml of glacial acetic acid and 20 ml of acetic anhydride was added 10 g (0.061 moles) of 3-keto-9-methyl-octahydronaphthalene (XXVII) (28). The mixture was stirred under nitrogen at 70-80°C for 24 hr. Most of the solvent was removed by distillation at aspirator pressure, 100 ml of water was added, and the mixture was extracted thoroughly with ether. The ether extracts were cautiously neutralized with solid sodium bicarbonate and dried over anhydrous sodium sulfate. The drying agent was removed by filtration, and the ether was removed in vacuo. The dark brown oil which remained was subjected to vacuum distillation to give starting material and the corresponding $\Delta^{1,4}$ compound (10) boiling at 80-85°C/0.005 mm, followed by 5.22 g (39 percent) of the desired product XLI boiling at 100-130°C/0.005 mm. The following properties were observed for XLI. The ultraviolet spectrum of XLI showed λ_{Max}^{EtOH}

241 nm, ε 11,000. The infrared spectrum showed, among others, absorptions at $\nu_{Max}^{CHCl_3}$ 1740 (ester carbonyl), 1686 (α,β unsaturated ketone) and 1619 cm^{-1} (conjugated double bond). The nmr spectrum of XLI showed absorptions at $\delta_{TMS}^{CCl_4}$ 1.25 (s, 0.6H, 9-CH_3), 1.38 (s, 0.4 H, 9-CH_3), 2.07 (s, 3H, -OCH_3 5.23 (t-broad, 1H, 2-H), 5.62 (s-broad, 0.4H, 4-H), and 5.67 (s-broad, 0.6H, 4-H). Analytical: Calculated: C 70.24, H 8.16, Found: C 70.09, H 8.16.

Saponification and Oxidation of XLI; Preparation of 2-Methoxy-3-keto-9-Methyl-$\Delta^{1,4}$-hexahydronaphthalene (XLII)

The procedure of Rao and Axelrod (36) was employed for the oxidation of XLI. A solution of 2.26 g (0.01 moles) of the keto-acetate XLI in 150 ml of methanol was treated with 1.2 g (0.022 moles) of potassium hydroxide dissolved in 10 ml of water. The resulting reaction mixture was stirred overnight at room temperature while a thin stream of oxygen was bubbled through the yellow solution using a fritted cylinder. The reaction mixture was then evaporated to near dryness, the residue was diluted with 50 ml of water, and the aqueous solution was washed with several 50 ml portions of ether. The aqueous layer was then acidified with dilute hydrochloric acid and extracted thoroughly with ether. The ether extracts were dried over anhydrous sodium sulfate, the drying agent was removed by filtration, and the solvent was removed in vacuo to leave a viscous yellow oil. The oil was not further purified, but was dissolved in 100 ml of dry t-butyl alcohol stirred under nitrogen, and a solution of 0.45 g (0.115 gram-atoms) of potassium metal dissolved in 50 ml of dry t-butyl alcohol was added in a thin stream. The reaction mixture, which turned an orange-red, was stirred 0.5 hr at

which time 4 g (0.028 moles) of methyl iodide was added in a thin stream. The reaction mixture was heated to reflux 20 min at which time approximately 3/4 of the t-butyl alcohol was removed by distillation. Fifty milliliters of water was then added and the mixture was extracted with ether. The ether extracts were dried with anhydrous sodium sulfate, the drying agent was removed by filtration, and the ether was removed in vacuo to leave a yellow oil which crystallized on standing. Recrystallization from ether gave white platelets melting at 106.5-107°C. The compound was identified as 2-methoxy-3-keto-9-methyl-$\Delta^{1,4}$-hexahydronaphthalene (XLII) by analogy to the work of Baran (37), and by its spectral and analytical properties reported below. The ultraviolet spectrum of XLII showed λ_{Max}^{EtOH} 250 nm, ε 10,000. The infrared spectrum showed, among others, absorptions at $\lambda_{Max}^{CHCl_3}$ 1658 and 1635 (α,β unsaturated ketone) and 1615 cm^{-1} (conjugated double bond). The nmr spectrum showed absorptions at $\delta_{TMS}^{CCl_4}$ 1.28 (s, 3H, 9-CH_3), 3.62 (s, 3H, 2-OCH_3), 5.77 (s, 1H, 4-H), and 5.97 (s, 1H, 1-H). Analytical: Calculated, C 74.96, H 8.39, Found: C 74.75, H 8.23.

Irradiation of 2-Methoxy-3-keto-9-methyl-$\Delta^{1,4}$hexahydronaphthalene (XLII)

It was found that irradiation with either the 2537 Å source for an extended period of time (8 to 12 hr) or the 450 watt source in quartz for 1 to 3 hr accomplished the same result. The progress of the reaction could be followed by observing the disappearance of the starting material carbonyl absorption in the infrared while simultaneously observing the appearance of a new carbonyl absorption which, in fact, was the absorption due to the main product of rearrangement.

In a typical run 7.6 g (0.04 moles) of XLII was dissolved in 300 ml of 45 percent aqueous acetic acid and irradiated until the new carbonyl group infrared absorption had reached a maximum with respect to that of the starting material. After the irradiation was complete, the solvent was removed by lyophilization and the resulting dark brown oil was chromatographed over 150 g of silica gel. Elution with 150 ml each of hexane and 10 percent ether in hexane afforded no material on evaporation of each portion. Further elution with 150 ml each of 20, 30, and 40 percent ether in hexane gave a total of 0.235 g of a mixture of compounds which were not identified. Elution with 150 ml more of 40 percent ether in hexane and 300 ml of 50 percent ether in hexane gave a mixture of compounds weighing a total of 0.516 g, the major component of which was shown to be α-hydroxy dienone XLIII by comparison with the intermediate of the same structure prepared in synthesis of XLII. Elution with an additional 300 ml of 50 percent ether in hexane followed by 600 ml of 60 percent and 300 ml of 70 percent ether in hexane gave 4.69 g of recovered starting material. Elution with 300 ml of 80 percent ether in hexane, 300 ml of 90 percent ether in hexane, and 150 ml of 100 percent ether gave a total of 0.342 g of a mixture of starting material and a compound later identified as the desired product. Finally elution with 1000 ml of 100 percent ether gave 1.11 g (35 percent based on recovered starting material) of a pale yellow oil. Purification by three successive micro Hickman distillations gave an almost colorless oil boiling at 110-120°C/105mm (pot temperature). The mass spectrum showed a molecular ion at m/e 210. The ultraviolet spectrum

showed λ_{Max}^{EtOH} 257 nm, ε 6700. The infrared spectrum showed, among others, absorptions at $\nu_{Max}^{CHCl_3}$ 1712 (α,β unsaturated cyclopentanone), and 1628 cm^{-1} (conjugated double bond). The nmr spectrum showed absorptions at $\delta_{TMS}^{CCl_4}$ 0.92 (s, 3H, 6-CH_3), 1.80 and 2.58 (AB quartet, J_{AB}=18.5 Hz, 2H, 4α, 4βH), 3.57 (s, 3H, 2-OCH_3), and 6.22 (s, 1H, -H). Analytical: Calculated: C 68.54, H 8.63. Found: C 68.74, H 8.69. The material was identified as 2-methoxy-3-keto-6α-methyl-6β-hydroxy-(4.5)spirodecene-1 (XLIV) by the above spectral data and by analogy to the known spiro-ketone IV_g (6).

During chromatography of a subsequent run in which the 450 watt source was used a second spiro-ketone was isolated in approximately 3 percent yield on elution with 300 ml of 50 percent ether in hexane and was shown to have the structure 2-methoxy-3-keto-6α-methyl-6β-acetoxy(4:5)spirodecene-1 (XLV). This material was identified by analogy to the work of Powers (38) and by the following spectral properties. The ultraviolet spectrum of XLV showed λ_{Max}^{EtOH} 254 nm, ε 5900. The infrared spectrum showed, among others, absorptions at $\nu_{Max}^{CHCl_3}$ 1718 (α,β unsaturated cyclopentanone and acetate carbonyl), and 1630 cm^{-1} (conjugated double bond). The nmr spectrum showed absorptions at $\delta_{TMS}^{CCl_4}$ 1.40 (s, 3H, 5-CH_3), 1.92 (s, 3H, -OAc), 1.80 and 2.58 (AB quartet, J_{AB}=19 Hz, 2H, 4-H), 3.70 (s, 3H, 2-OCH_3), and 6.34 (s, 1H, 1-H). Exact Mass: Calculated: 252.1361, Found: 252.1372.

Preparation of 2-Acetoxy-3-keto-5,9-dimethyl-Δ^4-octahydronaphthalene (XLVI)

The method used for preparation of XLI was employed. To a solution of 72.6 g (0.41 moles) of 3-keto-5,9-dimethyl-Δ^4-octahydronaphthalene (XLVII), prepared according to the method of Marshall (39),

dissolved in 800 ml of glacial acetic acid containing 60 ml of acetic anhydride was added 300 g (0.68 moles) of lead tetraacetate. The reaction mixture was heated at 60°C for 36 hr after which time most of the acetic acid was removed by distillation at aspirator pressure. The brown mass remaining was diluted with 200 ml of water and extracted thoroughly with ether. The ether extracts were neutralized with sodium bicarbonate, washed with water, and dried over sodium sulfate. The drying agent was removed by filtration, and the solvent was removed in vacuo to leave a viscous yellow oil. The oil was subjected to vacuum distillation to give fractions boiling at 80-120°C/0.25 mm and at 120-140°C/0.25 mm. The former was shown to be a mixture of starting material and the corresponding $\Delta^{1,4}$ compound, while the latter was shown to be the desired product by the following spectral data and by spectral analogy to compound XLI. The material weighed 42.8 g (44 percent). The ultraviolet spectrum of XLVI showed λ_{Max}^{EtOH} 242 nm, ϵ 12,600. The infrared spectrum showed, among others, absorptions at $\nu_{Max}^{CHCl_3}$ 1750 (acetate carbonyl), 1691 (α,β unsaturated ketone), and 1615 cm^{-1} (conjugated double bond). The nmr spectrum showed absorptions at $\delta_{TMS}^{CCl_4}$ 1.05 (d-broad, 3H, 5-CH_3), 1.25 (s, 2H, 9-CH_3), 1.42 (s, 1H, 9-CH_3), 2.03 (s, 3H, 2-OAc), 5.25 (t-broad, 1H, 2α&β-H), and 5.62 (s-broad, 1H, 4-H). Analytical: Calculated: C 71.15, H 8.53, Found: C 70.89, H 8.40.

Saponification and Oxidation of XLVI

The procedure of Rao and Axelrod (36) was employed. To a solution of 42.8 g (0.18 moles) of XLVI dissolved in 300 ml of methanol

was added a solution of 30 g (0.54 moles) of potassium hydroxide in 100 ml of water. The yellow solution was stirred at room temperature for 24 hr while a thin stream of oxygen was bubbled through a fritted cylinder into the solution. The methanol was partially removed in vacuo, and the reaction mixture was diluted with an equal volume of water. The aqueous solution was then washed thoroughly with ether, acidified with dilute hydrochloric acid, and the acidified aqueous solution was extracted thoroughly with ether. The ether extracts were washed once with saturated brine and dried over anhydrous sodium sulfate. The drying agent was removed by filtration and the ether was removed in vacuo to afford 33.2 g (96 percent) of crude XLVIII. The material was not further purified, but was used directly in the next step below.

Methylation of XLVII to give 2-Methoxy-3-keto-5,9-dimethyl-$\Delta^{1,4}$-hexahydronaphthalene (XLIV)

To a solution prepared from 28.5 g (0.73 gram-atoms) of potassium metal and 1000 ml of dry t-butyl alcohol stirred under nitrogen was added, in a thin stream, a solution of 33.2 g (0.17 moles) of XLVIII dissolved in 200 ml of dry t-butyl alcohol. The solution was stirred for two hours, and 142 g (1 mole) of methyl iodide was added in a thin stream. The mixture was stirred an additional hour at room temperature, boiled under reflux for 0.5 hr, and approximately 500 ml of the t-butyl alcohol removed by distillation. The remaining solution was diluted with an equal volume of water and extracted thoroughly with ether. The ether extracts were washed once with 50 ml of 10 percent sodium hydroxide and with saturated brine and dried over anhydrous sodium sulfate.

The drying agent was removed by filtration, and the ether was removed in vacuo to leave 23 g (64 percent) of a yellow oil which crystallized on standing. Recrystallization from ether-hexane gave white prisms melting at 82.5-83°C. The ultraviolet spectrum showed λ_{Max}^{EtOH} 251 nm, ε 11,300. The infrared spectrum showed, among others, absorptions at $\nu_{Max}^{CHCl_3}$ 1655 and 1635 (α,β unsaturated ketone) and 1610 cm^{-1} (conjugated double bond). The nmr spectrum showed absorptions at $\delta_{TMS}^{CCl_4}$ 1.10 (d, J=6 Hz, 3H, 5-CH_3), 1.25 (s, 3H, 9-CH_3), 3.57 (s, 3H, 2-OCH_3), 5.74 (s, 1H, 1-H), and 5.90 (d, J=1.7 Hz, 1H, 4-H). Analytical: Calculated: C 75.69, H 8.79, Found: C 75.44, H 8.61. On the basis of the above spectra and by analogy to XLII the material was identified as XLIX.

Irradiation of 2-Methoxy-3-keto-5,9-dimethyl-$\Delta^{1,4}$-hexahydronaphthalene (XLIX)

As was reported in the case of compound XLII either the 2537 Å source or the high pressure source (450 watts) could be used to effect the desired transformation of XLII to L. The progress of the transformation could also be monitored in the same fashion as described for the rearrangement of XLII. In a typical example 23 g (0.112 moles) of XLIX was irradiated for five hours with the 450 watt source at a concentration of 2 g per 250 ml of 45 percent acetic acid-water. Twelve grams of the material was chromatographed over 240 g of silica gel. Elution with 300 ml each of hexane, and 5, 10, 20 and 30 percent ether in hexane gave portions containing only small amounts of mixtures of compounds. Elution with 300 ml each of 40 and 50 percent ether in hexane gave a total of 1.23 g of the α-hydroxy dienone XLVII. This

compound was identified by comparison to the intermediate of the same structure prepared in the synthesis of XLIX. Further elution with 300 ml more of 50 percent ether in hexane followed by 900 ml of 60 percent ether in hexane and 600 ml of 70 percent ether in hexane gave only mixtures of oily materials which had no clearly defined spectral characteristics. Elution with 900 ml of 80 percent ether in hexane gave 1.83 grams of the starting material XLIX. Elution with an additional 300 ml of 90 percent ether in hexane gave a mixture of starting material and a compound later identified as L. Finally elution with 600 ml of 100 percent ether and 600 ml of 50 percent methanol in ether gave 2.26 grams of L. The remaining 11 g of crude photo product was chromatographed over another 240 g of silica gel in a manner analogous to that described above. The total yield of L was 5.64 g (28 percent based on 4.52 g recovered starting material). The structure of L was corroborated by analogy to IV_g (6), XL, and XLIV and by the following properties. The mass spectrum showed a molecular ion at m/e 224. The ultraviolet spectrum showed λ_{Max}^{EtOH} 258 nm, ε 8,300. The infrared spectrum of L showed, among others, absorptions at $\nu_{Max}^{CHCl_3}$ 1711 (α,β unsaturated cyclopentanone), 1626 (conjugated double bond), 1460, 1381, and 1351 cm^{-1} The nmr spectrum of L showed absorptions at $\delta_{TMS}^{CDCl_3}$ 0.72 (d, J=6 Hz, 3H, 10-CH_3), 1.05 (s, 3H, 6-α-CH_3), 2.16 and 2.72 (AB quartet, J_{AB}=19.5 Hz, 2H, 4-H), 3.75 (s, 3H, 2-OCH_3), and 6.33 (s, 1H, 1-H). Analytical: Calculated: C 69.64, H 8.93, Found: C 69.38, H 8.70. These properties support the structure 2-methoxy-3-keto-6α, 10α-dimethyl-6β-hydroxy-[4:5]spirodecene-1(L).

Lithium Aluminum Hydride Reduction of XLIV

To a solution of 0.114 g (0.003 moles) of lithium aluminum hydride stirred in 15 ml of anhydrous ether under nitrogen was added dropwise 0.197 g (0.001 moles) of XLIV dissolved in 10 ml of anhydrous ether. After the addition was complete the reaction mixture was heated to reflux for 1 hr, allowed to cool to room temperature, and stirred for an additional 2 hr. At the end of 2 hr a saturated solution of sodium sulfate was added dropwise until approximately 15 ml had been added. The layers were then separated, the aqueous layer was extracted with ether, and the combined organic layers were washed once with 10 ml of saturated brine. The solution was dried over anhydrous sodium sulfate, the drying agent was removed by filtration, and the solvent was removed *in vacuo*. The infrared spectrum of the oil remaining showed, as the only absorption of significance, $\nu_{Max}^{CHCl_3}$ 1650 cm^{-1} (double bond). The material was assigned the structure LI on the basis of this infrared spectrum and an nmr spectrum consistent with the proposed structure.

Reaction of LI with p-Toluenesulfonyl Chloride and the Attempted Reduction of The Resulting Tosylate

The oil prepared as described above was dissolved in dry pyridine, and the solution was cooled to 0°C. To the cold solution was added 0.274 g (0.0015 moles) of p-toluenesulfonyl chloride. The solution was stored at -10°C for 50 hr after which time the pyridine was removed *in vacuo* in the absence of heat. The reaction mixture was not further purified but was dissolved in dry THF and added slowly to a solution of 0.114 g (0.003 moles) of lithium aluminum hydride dissolved in 25 ml of dry THF stirred under nitrogen. The solution was heated to

reflux for 1 hr, allowed to cool to room temperature, and stirred for an additional 2 hr. Water (25 ml) was added, and the reaction mixture was thoroughly extracted with two 50 ml portions of ether. The ether solution was washed with 20 ml of 10 percent sodium hydroxide and 20 ml of saturated brine and dried over anhydrous sodium sulfate. The drying agent was removed by filtration, and the solvent was removed *in vacuo* to leave a brown oil. The nmr spectrum of the oil, while showing similarities to the spectrum of XLIV, was notable in the near absence of an absorption which would correspond to a methoxyl group at C-2 of the expected compound. Distillation of the oil in a micro-Hickman still afforded a small amount of a yellow oil. The nmr spectrum of this oil again was notable in the complete absence of an absorption which could be attributed to the methoxyl group of the expected compound.

Dehydration of XLIV with Thionyl Chloride

To a solution of 0.784 g (0.00037 moles) of XLIV dissolved in 1 ml of pyridine cooled to 0°C in an nmr tube was added 0.500 g of thionyl chloride. The material was allowed to react for 25 min at 0°C while the nmr spectrum was scanned rapidly every 10 min until the starting material could be no longer observed. The reaction mixture was then poured slowly into 30 ml of a slurry of ice and water, with stirring and the aqueous solution which resulted was thoroughly extracted with two 50 ml portions of ether. The combined ether extracts were washed with water, dried over anhydrous sodium sulfate, and the drying agent was removed by filtration. The ether was removed *in vacuo* to leave a dark brown oil. The oil was chromatographed over 2 g of silica

gel. Elution with 20 ml each of hexane and 5 and 10 percent ether in hexane gave oily materials which showed no carbonyl absorption in the infrared spectrum. Elution with 20 ml each of 30 and 50 percent ether in hexane gave a viscous yellow oil which exhibited the following spectral characteristics consistent with the desired structure LII. The infrared spectrum showed among others, absorptions at $\nu_{Max}^{CHCl_3}$ 1712 (α,β unsaturated cyclopentanone) and 1626 cm^{-1} (conjugated double bond). The nmr spectrum showed absorptions at $\delta_{TMS}^{CCl_4}$ 1.50 (d (unresolved), 3H, 5-CH_3), 2.09 and 2.26 (AB quartet, J_{AB}=19 Hz, 2H, 4-H), 3.65 (s, 3H, 2-OCH_3), 5.42 (m, 1H, 7-H), and 6.00 (s, 1H, 1-H). The 100 MHz nmr* spectrum showed absorptions at $\delta_{TMS}^{CCl_4}$ 1.52 (d, J=0.5 Hz, 3H, 5-CH_3), 2.08 and 2.25 (AB quartet, J_{AB}=19 Hz, 2H, 4-H), 3.68 (s, 3H, 2-OCH_3), 5.48 (m, 1H, 6-H), and 6.03 (s, 1H, 1-H).

Dehydration of L with Phosphorous Oxychloride

To a solution of 0.500 g (0.0023 moles) of L dissolved in 10 ml of dry pyridine stirred under nitrogen was added 2 ml of phosphorus oxychloride. The reaction mixture was stirred at room temperature for 1.5 hr followed by heating to 80°C for 0.5 hr. The reaction mixture was cooled to room temperature and water was cautiously added dropwise until a visible reaction no longer ensued. The mixture was then extracted thoroughly with ether, the ether extract was dried over anhydrous sodium sulfate, and the drying agent was removed by filtration. Solvent removal in vacuo gave a dark brown oil which was subjected to micro-

*The author would like to thank Professor R. H. Cox of the University of Georgia for obtaining this spectrum

Hickman distillation to give a pale yellow viscous oil. Glc analysis showed the oil to be made up of two compounds. Spectral properties of the material suggested that it was made up of an approximately 1:1 mixture of unreacted starting material and the desired product LIII.

Dehydration of L with Thionyl Chloride

To a solution of 2.26 g (0.101 moles) of L dissolved in 40 ml of dry pyridine stirred under nitrogen in an ice-salt bath was added 8 ml of thionyl chloride at such a rate that the temperature remained below 7°C. The reaction mixture was stirred for 0.5 hr at which time water was cautiously added dropwise so that the temperature remained below 20°C. Fifty milliliters of water was then added and the brown solution was thoroughly extracted with ether. The ether extracts were washed with saturated sodium chloride and dried over anhydrous sodium sulfate. The drying agent was removed by filtration, and the ether was removed in vacuo to leave a dark brown oil. Micro-Hickman distillation of the oil gave 0.756 g (36 percent) of a pale yellow, viscous oil whose structure was assigned that of 2-methoxy-3-keto-6α, 10-dimethyl-(4.5)-spirodeca-1,6-diene (LIII) on the basis of the following data. The ultraviolet spectrum of LIII showed λ_{Max}^{EtOH} 256 nm, ε 7900. The infrared spectrum showed, among others, absorptions at $\nu_{Max}^{CHCl_3}$ 1712 (α,β unsaturated cyclopentanone), 1623 (conjugated double bond), 1380, 1349, and 982 cm^{-1}. The nmr spectrum showed absorptions at $\delta_{TMS}^{CCl_4}$ 0.90 (d, J=6 Hz, 3H, 10-CH_3), 1.52 (d (unresolved), 3H, 6-CH_3), 2.20 and 2.32 (AB quartet, J_{AB}=19 Hz, 2H, 4-H), 5.52 (m, 1H, 7-H), and 6.22 (s, 1H, 1-H). Exact Mass: Calculated: 206.1307, Found: 206.1351.

Preparation of the Semicarbazone of LIII

To a solution of 0.075 g (0.00032 moles) of LIII dissolved in 5 ml of 95 percent alcohol and 5 ml of water was added 0.200 g of semicarbazide hydrochloride and 0.300 g of sodium acetate. The reaction mixture was heated on the steam bath for 0.5 hr and allowed to cool. The solvent was partially removed, and on cooling and scratching with a glass rod, white crystals were deposited. In all 0.061 g (68 percent) of a material melting 199-203°C with decomposition was collected.

Attempted Wolff-Kishner Reduction of the Semicarbazone of LIII

The procedure of Cram (40) was followed. To a solution of 0.023 g (0.00025 moles) of potassium t-butoxide stirred under nitrogen in 1 ml of dry dimethyl sulfoxide was added dropwise 0.061 g (0.00023 moles) of the semicarbazone of LIII dissolved in 1 ml of dimethyl sulfoxide. The brown solution was stirred for 7 hr. At the end of 7 hr, 3 ml of water was added, and the solution extracted with 25 ml of ether. The ether extracts were washed twice with 5 ml of water and dried over anhydrous sodium sulfate. The drying agent was removed by filtration and the ether was evaporated in vacuo to yield a solid which was spectrally identical to the starting material.

A second attempt to reduce the semicarbazone was also unsuccessful. The procedure used is described below. The recovered semicarbazone was dissolved in 20 ml of ethylene glycol, and the solution was distilled until the boiling point of the distillation reached 197°C The solution was then cooled, 0.020 g (0.00087 gram-atoms) of sodium metal was added, and the reaction mixture was again heated to reflux for one hour. The

solvent was partially removed at aspirator pressure, water was added, and the reaction mixture was extracted with 30 ml of chloroform. The combined chloroform extracts were washed once with 10 ml of water and dried over anhydrous sodium sulfate. The drying agent was removed by filtration, and the solvent was removed *in vacuo* to leave a dark brown oil. The nmr and ir spectra of the oil showed the presence of a material with properties resembling LIII, but none of the desired deoxy compound could be detected.

Attempted Wolff-Kishner Reduction of L*

To a solution of 0.285 g (0.00127 moles) of L dissolved in 10 ml of dry ethylene glycol stirred under nitorgen was added 0.2 g (*ca.* 0.0051 moles) of 95 precent hydrazine. The solution was heated to boiling, and was distilled until the boiling point reached 140°C. The solution was cooled at this point to *ca.* 60°C and 0.2 g (*ca.* 0.005 moles) of solid potassium hydroxide was added. The solution was again distilled until the head temperature reached 150°C, distillation was stopped, and the reaction mixture was boiled under reflux for one hour. The solution was cooled to room temperature, and 10 ml of water was added. The resulting mixture was then extracted thoroughly with ether, washed with water, and dried over anhydrous sodium sulfate. The drying agent was removed by filtration, and the solvent was removed *in vacuo* to leave a dark brown oil. The infrared spectrum of the crude reaction product

---

*The author would like to thank Professor Pierre Crabbe for suggesting this procedure.

showed no absorption in the carbonyl region. The nmr spectrum showed an absence of absorptions in the region 4.0 to 7.0 ppm along with a multiplicity of absorptions in the region 3.4 to 3.7 ppm.

Attempted Wolff-Kisner Reduction of LIII

To a solution of 0.166 g (0.0008 moles) of LIII dissolved in 5 ml dry ethylene glycol stirred under nitrogen was added 0.1 g of 95 percent hydrazine (ca. 0.0032 moles). The solution was heated to boiling and distilled until the head temperature was 120°C, cooled to ca. 60°C and 0.1 g of solid potassium hydroxide was added. The solution was again heated to boiling and distilled until the head temperature reached 120°C and then boiled under reflux for one hour. The reaction mixture was cooled, and 10 ml of water added. The mixture was then extracted thoroughly with 30 ml of ether, and the ether extract was washed with 10 ml of water and dried over anhydrous sodium sulfate. The drying agent was removed by filtration and the solvent was removed in vacuo to leave a brown oil. Although the infrared spectrum showed the absence of a carbonyl absorption, the nmr spectrum indicated that the material contained only small amounts of compounds containing a methoxyl group.

Lithium Aluminum Hydride Reduction of LIII, Normal Addition

Compound LIII (0.176 g, 0.00085 moles) in 15 ml of anhydrous ether was added dropwise to a solution of 0.076 g (0.002 moles) of lithium aluminum hydride in 20 ml of anhydrous ether stirred under nitrogen. After addition was complete, the reaction mixture was heated to boiling for one hour, cooled to room temperature, and stirred an

additional two hours. A saturated aqueous solution of sodium potassium tartrate was added dropwise until no further precipitation was observed; the reaction mixture was then filtered. The precipitate was washed with 20 ml of ether, and the ether layers were combined and washed with saturated sodium chloride solution. The solution was then dried over anhydrous sodium sulfate, the drying agent was removed by filtration, and the ether was removed *in vacuo* to leave a pale yellow oil weighing 0.113 g. The oil was identified as a 1:1 mixture of the C-3 epimers of 2-methoxy-3-hydroxy-6,10-dimethyl(4.5)spirodeca-1,6-diene (LIV), along with *ca.* 20% of a third compound presumed to be the product of 1,4 reduction by the following properties. The infrared spectrum showed, among others, absorptions at $\nu_{Max}^{CHCl_3}$ 3590 (hydroxyl), 1744 (saturated cyclopentanone), 1649 (olefin), 1460, 1375 and 1042 cm^{-1}. The nmr spectrum showed absorptions at $\delta_{TMS}^{CCl_4}$ 0.80 and 0.88 (d, J=6 Hz, 3H, 10-methyl groups), 1.30 and 1.47 (d, J=1.5 Hz, 3H, 6-methyl groups), 3.60 (s, 3H, 2-OCH_3), 4.33 (s, 1H, 1-H), 4.58 (t-broad, J=5 Hz, 1H, 3α and βH), and 5.32 (s-broad, 1H, 7H). Exact Mass: Calculated: 208.1463, Found: 208.1418.

Preparation of a Standard Solution of Lithium Aluminum Hydride

One gram of lithium aluminum hydride suspended in 30 ml of anhydrous ether was allowed to stand with occasional stirring for two hours. The solution was then filtered through a sintered glass funnel under nitrogen. The amount of reagent in the clear colorless solution was determined by adding the solution dropwise to water and measuring the volume of hydrogen evolved. From this it was calculated that a

solution prepared in the manner described contained approximately 0.0006 moles of lithium aluminum hydride per milliliter of liquid.

Lithium Aluminum Hydride Reduction of LIII, Inverse Addition

To a solution of 0.298 g (0.0014 moles) of LIII dissolved in 30 ml of anhydrous ether stirred at 0°C under nitrogen was added dropwise 0.6 ml of the standard solution, described in the previous experiment, dissolved in 10 ml of anhydrous ether. The reaction mixture was stirred for two hours while the temperature was maintained at 0°C and one hour while the temperature was allowed to rise to room temperature. The reaction was quenched by the dropwise addition of a saturated solution of sodium potassium tartrate until no further precipitation could be detected. The reaction mixture was filtered. The precipitate was washed with ether and the ether washings were combined with the filtrate. The material was then dried over anhydrous sodium sulfate, the drying agent was removed by filtration, and the solvent was removed in vacuo to leave 0.281 g (93 percent) of LIV whose properties have been described earlier.

Reaction of LIV with Acetic Anhydride/Pyridine

To a solution of 0.511 g (0.0025 moles) of LIV dissolved in 20 ml of dry pyridine stirred under nitrogen at room temperature was added 3.7 g of acetic anhydride. The reaction mixture was stirred for 24 hr at room temperature, 4 ml of water was added, and the solution was stirred an additional 1.5 hr at room temperature. An additional 10 ml of water was added and the reaction mixture was thoroughly extracted with 2 x 50 ml of ether. The combined ether extracts were washed with saturated sodium

bicarbonate solution and saturated brine, and dried over anhydrous sodium sulfate. The drying agent was removed by filtration, and the solvent was removed in vacuo to leave a non-viscous oil which smelled strongly of pyridine. These last traces of pyridine were removed under high vacuum to give 0.566 g (92 percent) of a clear colorless oil which was identified as a mixture of the C-3 epimers of 2-methoxy-3-acetoxy-6,10-dimethyl(4·5)spirodeca-1,6-diene(LV) by the following properties. The infrared spectrum of LV showed, among others, absorptions at $\nu_{Max}^{CHCl_3}$ 1726 (ester carbonyl) 1648 (olefin), 1366, and 1025 cm^{-1}. The nmr spectrum of of LV showed absorptions at $\delta_{TMS}^{CCl_4}$ 0.85 and 0.90 (d, J=6 Hz, 3H, 10-methyl groups), 1.52 and 1.60 (d, J=1.5 Hz, 3H, 6-methyl groups), 1.97 (s, 3H, 3-OAc), 3.58 (s, 3H, 2-OCH_3), 4.55 (s, 1H, 1-H), 5.36 (m, 1H, 7-H), and 5.40 and 5.56 (t, J=4 Hz, 1H, 3α and βH). Exact mass: Calculated: 250.1568, Found: 250.1503.

Attempted Hydrolysis of LV

To 0.100 g of oxalic acid dissolved in 2 ml of water was added a solution of 0.500 g of LV dissolved in 5 ml of methanol. The reaction mixture was stirred for 0.5 hr. At the end of this time solid sodium bicarbonate was added until carbon dioxide evolution ceased, 5 ml more water was added, and the mixture was extracted thoroughly with 25 ml of ether. The ether extracts were washed with saturated brine and the solvent was removed in vacuo to remove the methanol. The material was again dissolved in 25 ml of ether, and dried over anhydrous sodium sulfate, the drying agent was removed by filtration, and the ether was evaporated to leave a yellow oil. Spectral analysis of the oil revealed it to be unreacted starting material. The experiment was repeated as described,

but the reaction time was extended to two hours. Work up again gave only unreacted starting material. The reaction was repeated a third time using 10 ml of methanol and 0.200 g of freshly sublimed oxalic acid. Again work up revealed no reaction. The experiment was repeated a fourth time as follows. p-Toluenesulfonic acid (0.100 g) was dissolved in 1 ml of water, and compound LV was added in 4 ml of dioxane. The reaction mixture was stirred for 21 hr. Work up in the above manner gave a yellow oil which was shown to consist mainly of unreacted LV.

Attempted Preparation of the Ethylene Dithio-Ketal of XLIV

To a solution of 0.215 g (0.001 moles) of XLIV dissolved in 20 ml of dry benzene was added 0.480 g (0.005 moles) of ethanedithiol followed by 1 ml of boron trifluoride-etherate. The reaction mixture was stirred for 0.5 hr, neutralized with saturated sodium bicarbonate solution, and extracted with ether. The ether extracts were washed with dilute sodium hydroxide and water and dried in the usual manner. Removal of the drying agent by filtration and evaporation of the solvent gave a brown oil. The infrared spectrum indicated the absence of any absorption in the region 1600 to 1800 cm^{-1}; however, the nmr spectrum of the material showed no absorption corresponding to the enol ether methyl group which would be part of the desired product. Instead there was a broad intense absorption around 3.3-3.5 ppm which was attributed to the protons on the ethylene dithioketal functionality. Mass spectral examination of the material revealed a peak at m/e 348 corresponding to the bis-dithioketal.

The reaction was repeated as follows. A solution of 0.199 g (0.00095 moles) of XLIV and 0.098 g (0.001 moles) of ethanedithiol in 20 ml of dry ether stirred under nitrogen was cooled to 0°C. To the cold solution was added dropwise over a period of 2.5 hr 0.5 ml of boron trifluoride etherate dissolved in 20 ml of dry ether. The cooling bath was removed, and the reaction mixture was allowed to warm to room temperature while stirring was maintained (ca. 0.5 hr). The reaction mixture was washed with dilute sodium hydroxide and with water and dried in the usual manner. Evaporation of the solvent gave a yellow oil whose spectral properties indicated it to consist primarily of starting material.

Hydrogenation of XLIV Using Palladium on Carbon

A solution of 0.417 g (0.002 moles) of XLIV in 20 ml of absolute ethanol containing 0.100 g of 5 percent palladium on carbon was subjected to 40 psig of hydrogen for 6 hr. Removal of the catalyst by filtration and evaporation of the solvent in vacuo gave a pale yellow oil. Spectral examination of the material indicated that the reaction had proceeded only partially to completion, therefore the reaction was continued for an additional 48 hr using 95 percent ethanol as the solvent. Workup of the reaction mixture as described gave a viscous yellow oil with the following properties. The infrared spectrum of the oil showed, among others, an absorption at $\nu_{Max}^{CHCl_3}$ 1745 cm^{-1} (saturated cyclopentanone). The nmr spectrum showed absorptions at $\delta_{TMS}^{CCl_4}$ 1.17 (s, 3H, 6-CH_3), 1.44 (s-broad, 8H, 7,8,9,10-H), and 3.42 (s, 3H, 2-OCH_3). The mass spectrum showed a molecular ion at m/e 212. These properties suggest that the compound was the desired dihydro XLIV.

Hydrogenation of Dihydro XLIV Using Platinum Oxide

The material obtained in the previous experiment was shaken with 0.020 g of platinum oxide suspended in 20 ml of 95 percent ethanol at 40 psig for 64 hr. Filtration of the reaction mixture followed by evaporation of the solvent in vacuo gave an oily material with the following properties. The infrared spectrum showed the absence of an absorption in region 1600-1800 cm^{-1}. The nmr spectrum showed absorptions at $\delta^{CCl_4}_{TMS}$ 1.15 (s, 3H, 6-CH_3), 1.43 (s-broad, 8H, 7,8,9,10-H), and 3.34 (s-broad, 3H, 2-α and β-OCH_3). The absorption for the C-3 protons was not well defined due to the presence of impurities which obscured its position.

Dehydration of Tetrahydro XLIV

The material obtained in the preceding experiment was dissolved in 5 ml of dry pyridine cooled to 0°C under nitrogen. Thionyl chloride, 1 ml, was added, and the reaction mixture was stirred in the cold for 2.5 hr. The reaction was cautiously quenched with 2 ml of cold water and the reaction mixture extracted with ether. The ether extracts were washed with saturated brine and dried in the usual manner. Evaporation of the solvent in vacuo gave a dark brown oil whose spectral properties indicated it was composed mainly of starting material. A second attempt to dehydrate the material resulted in an oil whose spectral properties were characteristic of a mixture of polymeric materials. Gas chromatographic analysis of the material showed it to be a complicated mixture of compounds.

Lithium/Ethyl Amine Reduction of LV and Hydrolysis of the Reaction Product

The general method of Henbest (41) was employed. to a solution of 0.105 g (0.0004 moles) of LV dissolved in 10 ml of dry ethylamine stirred under nitrogen was added 0.10 g (0.0014 gram-atoms) of lithium wire. The blue color formed in the immediate vicinity of the lithium was rapidly discharged. Stirring was continued until the blue color persisted for 10 min at which time solid ammonium chloride was added to destroy the excess lithium. The ethylamine was evaporated and the semi-solid material remaining was washed thoroughly with ether. The ether extracts were washed with saturated sodium bicarbonate solution and with saturated brine, and were dried in the usual manner. Evaporation of the solvent gave a brown oil whose spectral properties were not well defined but were suggestive of a mixture of compounds LVI and LVII. The nmr spectrum showed a low intensity absorption for the C-2-methoxyl group of LVI indicating that only a small amount of this compound was present. The infrared spectrum showed an absorption at 1729 and 1642 cm^{-1} indicating the presence of a saturated cyclopentanone ring and olefinic linkage respectively. The material was not further purified but was heated on the steam bath for 2 hr followed by stirring at room temperature over night in a solution of 5 ml of dioxane and 1 ml of water containing 0.100 g of oxalic acid. The reaction mixture was diluted with ether, washed with saturated sodium bicarbonate solution and with water, and dried in the usual manner. Evaporation of the solvent left a brown oil whose spectral properties were consistent with an impure mixture containing primarily LVII. The mass spectrum showed a molecular ion at m/e 178.

Lithium/Ethylamine Reduction of LV, Inverse Addition

To a solution of 0.316 g (0.0013 moles) of LV dissolved in 20 ml of dry ethylamine stirred under nitrogen was added dropwise a solution of 0.040 g (0.0057 gram-atoms) of lithium wire dissolved in ca. 20 ml of dry ethylamine. Addition was continued until the blue color persisted ca. 20 sec and an excess of solid ammonium chloride was added. The ethylamine was evaporated, and the semi-solid mass remaining was thoroughly washed with ether. The ether solution was not washed with water, but was immediately dried in the usual fashion. Removal of the solvent left 0.245 g (100 percent) of a yellow oil which exhibited the following properties. Glc analysis showed the oil to be greater than 95 percent homogeneous. The infrared spectrum of the material showed, among others, absorptions at $\nu_{Max}^{CHCl_3}$ 1645 (olefin), 1450, 1376, and 1352 cm^{-1}. The nmr spectrum showed absorptions at $\delta_{TMS}^{CCl_4}$ 0.78 (d, J=6 Hz, 3H, 10-CH_3), 1.49 (d, J=1.5 Hz, 3H, 6-CH_3), 3.45 (s, 3H, 2-OCH_3), 4.13 (t, J=1 Hz, 1H, 1-H), and 5.20 (m, 1H, 7-H). Exact Mass: Calculated: 192.1514, Found: 192.1540. On the basis of the above data the compound was identified as 2-methoxy-6,10-dimethyl-spiro(4.5)deca-1,6-diene (LVI).

Hydrolysis of LVI

A solution of 0.260 g (0.0013 moles) of LVI dissolved in 10 ml of methanol containing 4 ml of water and 0.050 g (0.0005 moles) of oxalic acid was stirred at room temperature for 0.5 hr. Saturated sodium bicarbonate solution, 5 ml, was added, and the reaction mixture was extracted with 1:1 benzene-ether. The organic extracts were dried in the usual manner, and the solvents were removed in vacuo to leave 0.253 g (100

percent) of a pale yellow oil. The material was identified as 2-keto-6,10α-dimethyl-spiro(4·5)dec-6-ene LVII by the following properties. Glc analysis showed the material to be composed of essentially one compound. The infrared spectrum of LVII showed, among others, absorptions at $\nu_{Max}^{CHCl_3}$ 1732 (saturated cyclopentanone), 1450, 1400, 1380, 1260, and 1163 cm^{-1}, and $\nu_{Max}^{Thin\ film}$ 1740, 1450, 1404, 1378, 1160, 900, and 800 cm^{-1}. The 60 MHz (see Appendix, Plate 1) spectrum showed absorptions at $\delta_{TMS}^{CCl_4}$ 0.93 (d, J=6 Hz, 3H, 10-CH_3), 1.65 (d, J=1.5 Hz, 3H, 6-CH_3), 2.15 and 2.16 (AB quartet, J_{AB}=-19 Hz, 2H, 1-α and β-H), 5.55 (m, 1H, 7-H). The position reported for the AB quartet was verified by the 100 MHz spectrum of LVII. Exact mass: Calculated: 178.1353, Found: 178.1357.

Preparation of 3-Keto-6β-hydroxy-6-10α-dimethylspiro(4·5)decane (LVIII)

A quanity of 0.283 g (0.0016 moles) of compound LIX, prepared according to the method of Kropp (6), was dissolved in 20 ml of 95 percent ethanol containing 0.050 g of 5 percent palladium on carbon and shaken for 16 hr with hydrogen under 30 psig. The catalyst was removed by filtration and the solvent was removed in vacuo to leave 0.283 g of a yellow oil which exhibited characteristics consistent with the structure LVIII and those of the ketone prepared by Marshall (42).

Preparation of 3-Keto-6,10α-dimethyl spiro(4·5)dec-6-ene (LX)

The procedure used for compound LIII was employed. Compound LVIII, 0.283 g (0.0014 moles), was dissolved in 20 ml of dry pyridine stirred at 0°C under nitrogen. One milliliter of thionyl chloride was added, and the reaction mixture was sitrred for 0.5 hr at 0°C. At the end of this time cold water was added cautiously to the reaction mixture,

and the brown solution was extracted thoroughly with ether. The ether extracts were washed with saturated brine and dried in the usual manner; the solvent was removed in vacuo to leave a yellow oil. The spectral properties of the oil were consistent with structure LX and identical to spectral properties of the known compound reported by Kropp (43). The infrared spectrum obtained as a liquid film exhibited the following absorptions: $\nu_{Max}^{Thin\ film}$ 1740 (saturated cyclopentanone), 1450, 1402, 1378, 1156, 900, and 800 cm^{-1}. The nmr spectrum of LX (See Appendix, Plate 2) showed absorptions at $\delta_{TMS}^{CCl_4}$ 0.93 (d, J=6 Hz, 3H, 10-CH_3), 1.65 (d, J=1.5 Hz, 3H, 6-CH_3) 2.10 and 2.24 (AB quartet, J_{AB}= -19 Hz, 2H, 3α and 3β-H), and 5.57 (m, 1H, 7-H).

Reaction of LVII with Lithium Acetylide

To a solution of lithium acetylide in liquid ammonia, prepared from 0.010 g (0.0014 gram atoms) of lithium wire in 20 ml of anhydrous ammonia containing a trace of ferric chloride through which dry acetylene had been passed for 0.5 hr, was added dropwise 0.250 g (0.0014 ml) of LVII in 10 ml of dry ether. The reaction mixture was stirred under nitrogen for one hour while a stream of acetylene was bubbled through the solution continuously. At the end of the reaction period, an excess of solid ammonium chloride was added, and the ammonia was evaporated from the flask. The semi-solid mass remaining was thoroughly extracted with ether, and the ether extracts were washed with water and dried in the usual manner. Removal of the solvent in vacuo left a yellow oil which was shown to be starting material.

Reaction of LVII With Sodium Acetylide

The reaction described in the previous experiment was repeated except that sodium acetylide was used instead of lithium acetylide and the reaction was continued for a total of 6 hr. Acetylene was bubbled through the reaction mixture for three of the six hours rather than for the entire period. Work up of the reaction mixture left a brown oil which exhibited the properties of starting material and polymeric materials.

Reaction of LVII With Lithium Acetylide-Ethylenediamine Complex

The method of Huffman (44) was employed. To a suspension of 0.828 g (0.009 moles) of lithium acetylide-ethylenediamine complex in 7.5 ml of dry dioxane saturated with dry acetylene was added dropwise over a period of 0.5 hr 0.160 g (0.009 moles) of LVII dissolved in 7.5 ml of dry dioxane under nitrogen. Acetylene was bubbled through the reaction mixture throughout the period of addition and for 0.5 hr afterwards. The reaction mixture was warmed to 35-40°C and stirring was continued for 22 hr. An excess of solid ammonium chloride was added followed by 2 ml of dilute hydrochloric acid. The reaction mixture was extracted with ether, and the ether extracts were washed twice with saturated brine. Drying in the usual manner followed by removal of the solvent left a brown oil. Although the nmr and mass spectral properties were not completely consistent with the desired compound LXI, the infrared spectrum showed an absorption in chloroform at 1730 (saturated cyclopentanone), and 3300 cm^{-1} (acetylenic terminal C-H stretching). The absorption at 1730 was less intense than the corresponding absorp-

tion in the starting material. No absorption was observed in the region 2000-2500 cm^{-1}.

Treatment of Crude LXI with Dowex 50W-X12 Resin (H^+ Phase)

To 1.35 g of Dowex 50W-X12 resin (H^+ Phase) under nitrogen was added the crude product from the preceding experiment dissolved in 5 ml of glacial acetic acid. Water, 0.45 ml, was added, and the reaction mixture was heated to boiling with stirring for 24 hr. The solution was cooled to room temperature, 25 ml of ether was added, and the mixture was washed with 20 percent sodium hydroxide solution until the wash was basic. The ether solution was then washed with saturated brine and dried in the usual fashion and the solvent was removed. Glc analysis revealed the oil remaining contained several different compounds but consisted of one major component. Spectral examination of the material gave only poorly defined results. The material was thus subjected to preparative glc, and the major component of the mixture was collected. Spectral data on the collected component show it to be identical to compound XLVII.

Treatment of LVII with Dowex 50W-X12 Resin (H^+ Phase)

Approximately 0.80 g (0.0045 mole) of LVII, one gram of Dowex 50W-X12 resin (H^+ Phase), 3 ml of water, and 0.5 ml of glacial acetic acid were heated to boiling under nitrogen for 24 hr. The reaction mixture was cooled to room temperature, ether was added and the mixture was washed with 20 percent sodium hydroxide solution until the wash was basic. The ether solution was then washed with saturated brine, dried in the usual fashion, and the solvent was removed to leave a dark brown

oil. Glc analysis of this material showed it to be a mixture of several components containing one major compound. This major component was collected by preparative glc. Spectral examination revealed that the material was identical to known XLVII.

CHAPTER IV

DISCUSSION OF RESULTS

As indicated in Chapter I, the purpose of the work described in this thesis was to investigate further the photochemical rearrangements of cross-conjugated cyclohexadienones and to apply these rearrangements to the synthesis of naturally occurring compounds having 5/7-fused and (4.5) spirodecane ring systems. The first part of the discussion will deal with the rearrangement of such systems, and the second part will be devoted to the synthetic work involving the products of the rearrangements.

Starting materials for preparing the required dienones were, without exception, based on an octalone system of the type XXVII (28). Compounds of the type XXVII are generally prepared by condensing a cyclohexanone moiety with an appropriate vinyl ketone or vinyl ketone precursor followed by cyclization, the necessary functional groups being introduced either as a part of the cyclohexanone before annelation or added onto the octalone system after ring closure. The second double bond of the diene chromophore is usually introduced as the last step in the synthesis of such compounds.

An exception to such a sequence is that leading to the dienone prepared by DeBardeleben in 1967 (10) in which the second double bond is introduced as part of the ring closure sequence. Preparation of XX, although being rather long, proceeded straightforwardly to give the

desired compound. Irradiation of this compound in the manner described followed by workup and chromatography of the reaction mixture gave 17 percent of the lactone XXI analogous to the lactone XXII reported by DeBardeleben (10) and 35 percent of the alcohol XXIII in analogy to the results reported by DeBardeleben (10) for the rearrangement of the acid Id. It was hoped that compound XXIII would be of use in the synthesis of α and β-vetivones. This will be discussed later.

Several approaches to 4-substituted dienones were investigated. In the first of these, compound XXVI was prepared from octalone XXVII using the general method of Wenkert (27) for generating and trapping the enolates of XXVII. An excess of compound XXVII was stirred with a suspension of sodium hydride in DME overnight so as to generate the equilibrium enolate LXII (27). This enolate was then carbonated by pouring a solution of the anion over solid carbon dioxide; however, this procedure gave reduced yields of the product. Presumably the presence of moisture, which could not be excluded from the reaction mixture when this method was employed, accounted for the difficulty. It was noted that if the reaction mixture was not made basic for a short time before acidification and esterification with diazomethane, reduced yields of XXVI were obtained. The initial product of carbonation is probably the sodium salt of the acid LXIII, which would be expected to decarboxylate spontaneously on acidification. If however, the material was treated with base prior to acidification the double bond would be expected to isomerize into conjugation to give compound LXIV. This compound should be stable to acid long enough to react successfully with diazomethane. Esterification with diazomethane proceeded satisfactorily when the wet

ether solution of the alkylating agent obtained on treating N-nitroso-N-methyl urea with base was used without further purification.

Unfortunately, all attempts to prepare the dienone XXVII from XXVI resulted in mixtures of double bond isomers which defied separation. Using DDQ as an oxidizing agent (6, 8, 10, 38) four different sets of conditions were employed in an attempt to selectively introduce a 1,2 double bond into XXVI. Both the reaction time and solvent were varied over a wide range but in all cases the ratio of compounds formed appeared to be essentially constant. All attempts to separate the mixture proved futile. These included both careful fractional distillation and column chromatography, separately and in combination. The mixture appeared to be made up of compounds XXVIII, XXIX, and XXX. It is known (45) that compounds of the type XXX are formed on treatment of similar systems with chloronil, a reaction closely related to the one under discussion. It is also known that treatment of XXVII with DDQ under strongly acidic conditions gives rise to linearly conjugated dienones of the type XXX. Powers (38) has found that treatment of compound LXVI with DDQ in benzene also gives rise to a mixture of the corresponding cross-conjugated and linearly conjugated dienones. The exact quantitative nature of the mixture XXVIII, XXIX, and XXX was not determined; however, a large predominance of any one isomer was not observed.

As in the preparation of XXVI, the starting material for preparation of XXXIII was the octalone XXVII. The method of Djerassi (31) was used to prepare XXXII from XXVII. Not unlike the case of XX, the procedure is long but proceeded straightforwardly to the desired compound. The method of Woodward (30) was employed to react ethyl formate with

XXXII in the presence of sodium methoxide to give 4-hydroxymethylene derivative, XXXI. This compound was then treated with DDQ according to the method of Debardeleben (10). The reaction proceeded smoothly and the desired dienone was obtained in satisfactory yield. It will be noted that an absorption at 3.80 ppm in the nmr spectrum of XXXIII has been assigned to the C-6 equatorial proton. This unusually low field absorption for an allylic proton may be due to the proximity of the C-4 formyl group to the C-6 proton. A similar observation has been made with respect to compound XXXVI as will be discussed later.

Irradiation was carried out in 45 percent acetic acid using the 450 watt source with a Pyrex filter. The reaction was continued for 1.5 hr to give what appeared by nmr to be a mixture of starting material and a small amount of its deconjugated isomer, compound LXVII. Distillation of this mixture gave a fraction still a mixture but greatly enriched in LXVII (ca. 1:1). Further irradiation of this distilled material for a short time with a 2537 angstrom source gave a material identical in its spectral properties to XXXIII. On standing overnight at 0°C in ether, the mixture obtained on distillation showed a slight reversion toward the initial composition observed after the first irradiation. It was observed that on extended irradiation of XXXIII with the 2537 angstrom source, only a mixture of intractable, polymeric oils were obtained. It is believed that the initial deconjugation is of a thermal origin rather than a photochemical one for the following reasons. Only a small amount of LXVII was observed after the irradiation, probably less than 10 percent, while a relatively large

amount, probably greater than 40 percent, was observed after distillation, which necessitated extensive heating. Since the irradiation was carried out in acidic media, and since the temperature of the reaction is ca. 30°C, a small amount of thermal deconjugation would, if thermodynamically favored be expected to occur. On the other hand, irradiation with the 2537 angstrom source was carried out at ca. 20°C again in acid solution. This temperature difference could account for a thermodynamic rather than photochemical reversal to give reconjugation. Additional information regarding this apparently facile equilibrium could have been obtained from studies on the effect of heat on XXXIII which had not been exposed to ultraviolet light; however, insufficient material was available for such studies.

The 4-cyanoenone (XXXIV) was also prepared from the formyl octalone, XXXI. The procedure of Kuehne (32) was followed (See Chart II). Compound XXXI was reacted with hydroxylamine hydrochloride in glacial acetic acid to give a crude product whose structure was believed to be that of the isoxazole, XXXV. Compound XXXV was not purified, but was reacted directly with sodium methoxide in dry benzene. Work up gave the desired XXXIV in 50 percent yield. This material was reacted with DDQ in the manner of Kissman (33) to give the dienone XXXVI. Attempts at preparing XXXVI in a manner similar to that used for XXXIII gave, on work up, only starting material. Since the rate of reaction of DDQ with systems of this type is considered to be dependent on the rate of enolization of the system, it was felt that XXXIV should be of the order of reactivity of XXXI. Apparently the extent of enolization of XXXIV is not great enough to give rise to a rate of reaction as large as that observed for compounds of the type XXXI, but it should be noted that the reaction time

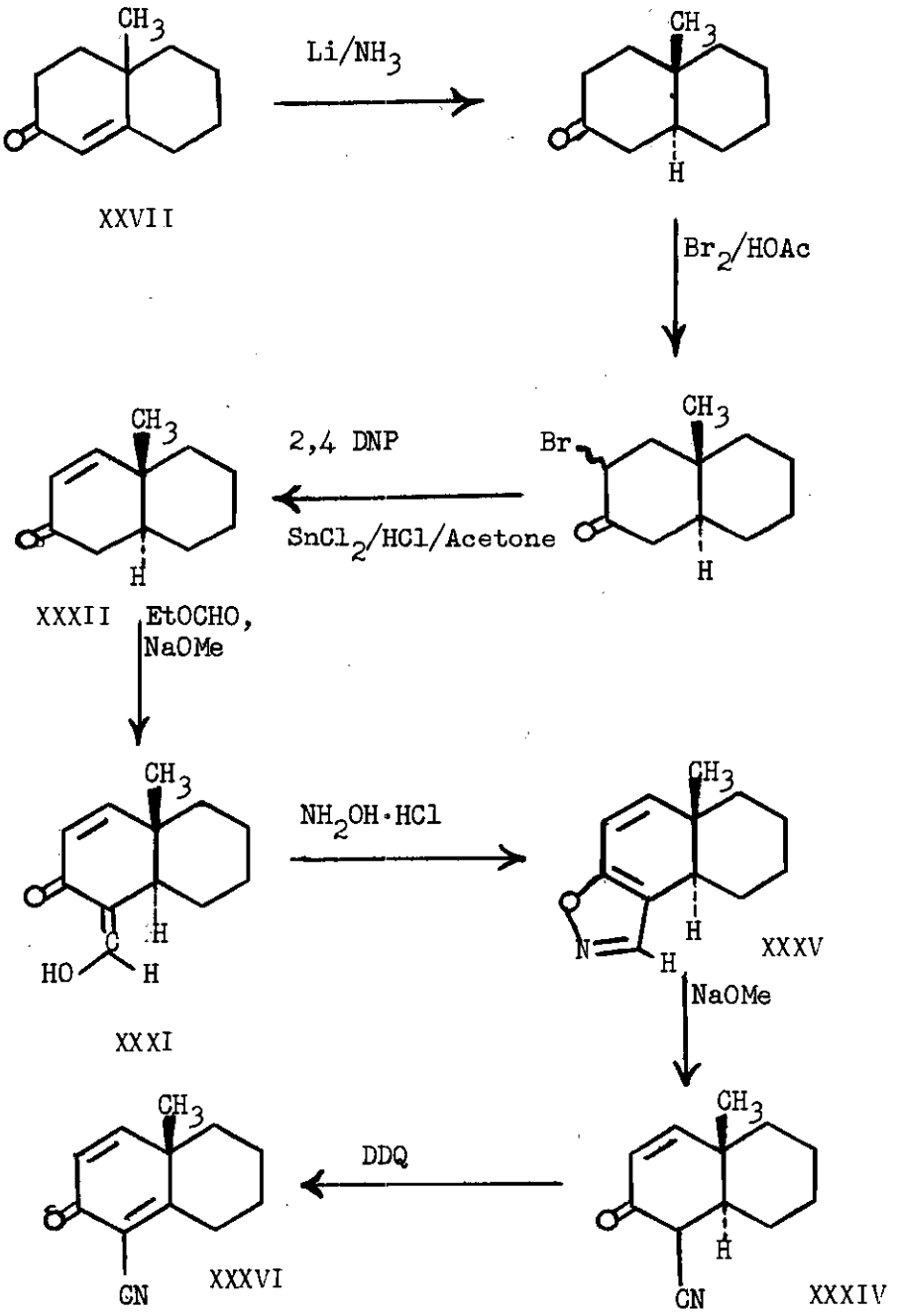


Chart II. Synthetic Route to 4-Cyanodienones.

required (ca. 12 hr) is only approximately one-third that required for compounds of the type XXVII where the enol content of the material is quite small. As was pointed out earlier with respect to XXXIII, compound XXXVI also exhibits an absorption in the nmr spectrum at unusually low field for an allylic proton which has been assigned to the C-6 equatorial proton. As in the earlier case, the proximity of the cyano group to this C-6 proton is felt to be the cause of this abnormal absorption.

Irradiation of XXXVI was conducted in 45 percent aqueous acid using the 450 watt source with a Pyrex filter. Work up of the reaction mixture gave a crude brown oil which was chromatographed over silica gel to give the spiro hydroxy ketone XL in 24 percent yield. Photolysis of XXXVI also gave two additional products. Isolated along with XL was a 3 percent yield of the phenol XXXVIII in direct analogy to the known phenol XXXVII obtained in other systems (2). Also isolated and tentatively identified was the hydroazulene XXXIX in 13 percent yield. The behavior of XXXVI with a cyano group at C-4 is in direct contrast to the findings of Debardeleben (10) on systems substituted with electron withdrawing groups at the 2 position in which he found products whose formation could be explained by cleavage of the mesoionic intermediate VIII in only one way. While it is possible that the 2-cyano compound might not exhibit the same behavior as the 2-ester and 2-acid, it was anticipated that the location of this group at C-4 would lead exclusively to the spirodecane structure. One explanation of these observations could lie in the fact that the cyano group simply does not sufficiently destabilize the resonance form of VIII which gives rise to hydroazulenes

to exclude a substantial contribution from this form. On the other hand, it is known that in such systems phenols usually arise from photolytic cleavage of lumiproducts (2). The fact that a 3 percent yield of the phenol was isolated indicates the probable intermediacy of a lumiproduct. Compound XXXIX could then also arise from solvolytic cleavage of this lumiproduct.

Compound XLI was prepared according to the method of Seeback (35). A solution of XXVII in glacial acetic acid containing a small amount of acetic anhydride was treated with an excess of lead tetraacetate at 70-80°C for 24 hr. Work up of the reaction mixture gave a 39 percent yield of the desired 2-acetoxy ketone, XLI. Along with XLI was formed an almost equal quantity of the dienone Ig (10). The mechanism for the formation of XLI reported by Henbest (47) is shown in chart III. It is probable that Ig arises from the loss of a β proton from the lead ester as shown in chart III. Various attempts were made to improve the yield of XLI to no avail. Changes in the reaction time and temperature had little, if any, effect on the amount of XLI obtained, however, longer reaction times or higher temperatures did slightly increase the amount of Ig obtained. The method of Henbest (46) was also tried. This consisted of dissolving the carbonyl compound to be acetylated in either ether or benzene. To this solution a catalytic amount of boron trifluoride etherate and the required amount of lead tetraacetate was added. The reaction mixture was stirred at room temperature until starch iodide paper indicated that all of the lead tetraacetate had been consumed. Although for several cases Henbest reported vastly improved yields over those obtained by the method of Seeback, only starting material was

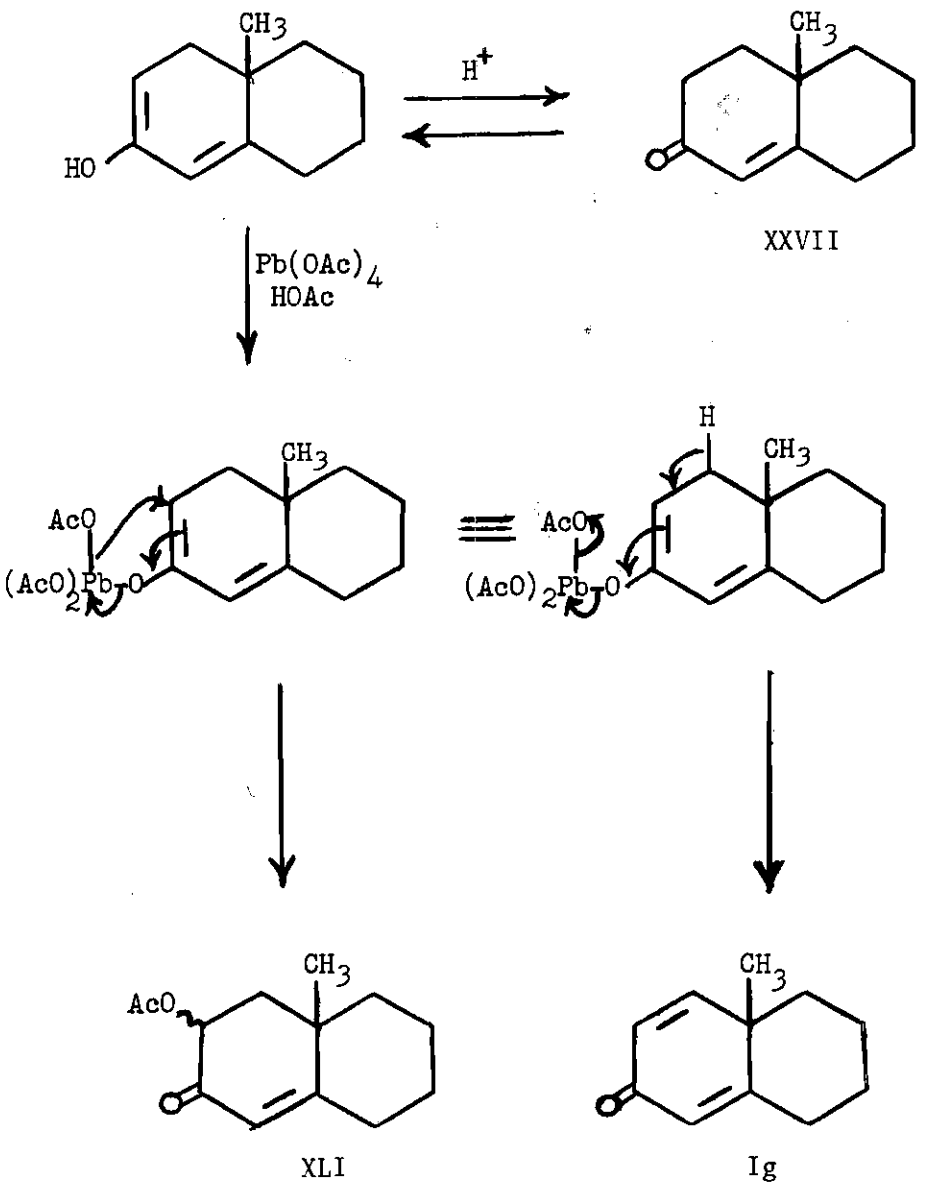
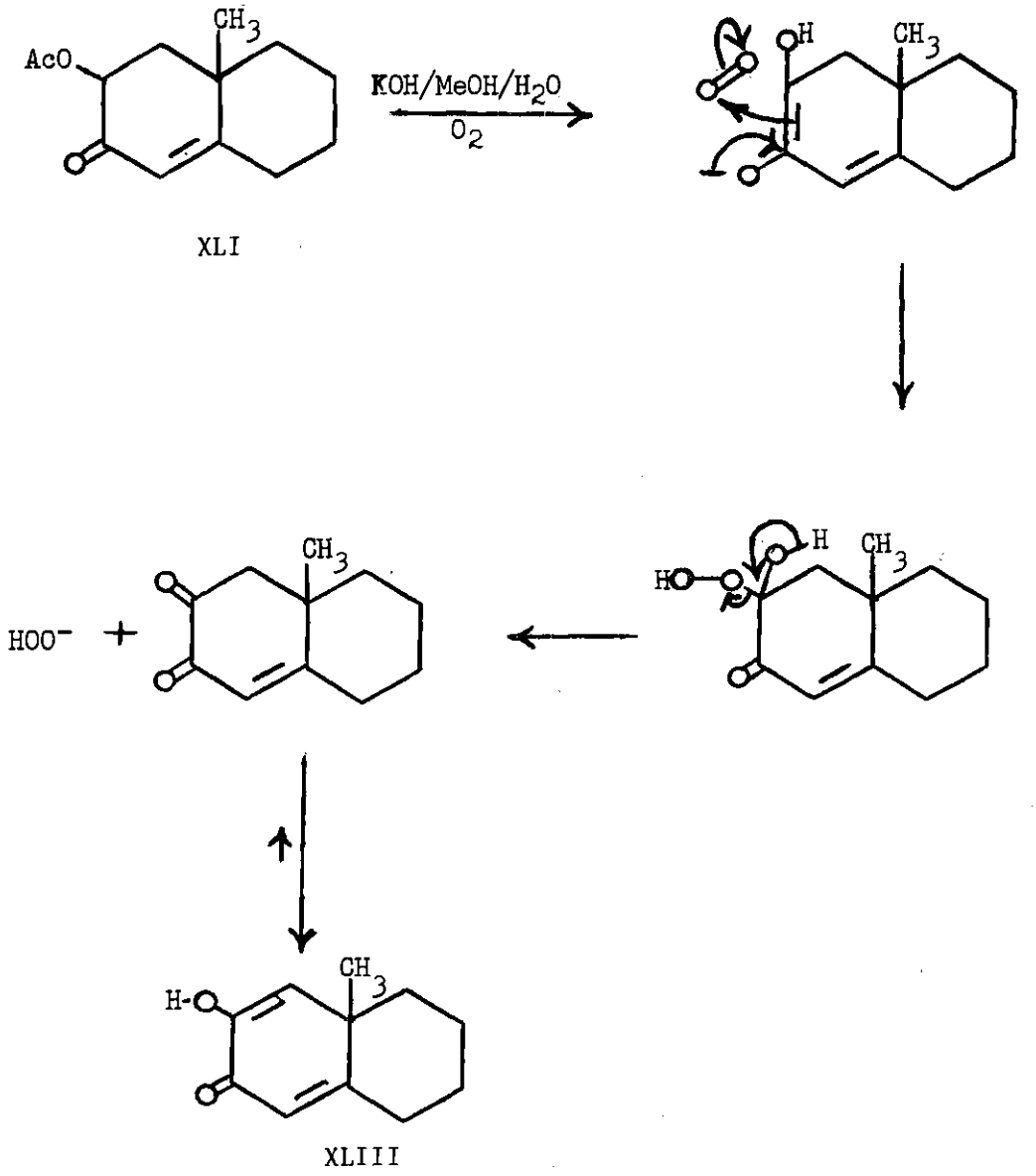


Chart III. Mechanism of Lead Tetraacetate Oxidation of Ketones.

recovered in attempts to prepare XLI by the identical procedure.

The general procedure of Rao and Axelrod (36) was employed for the preparation of XLIII. The acetate XLI was stirred with an aqueous methonolic solution of potassium hydroxide while a thin stream of oxygen was bubbled through the solution. The 2-hydroxy dienone formed was not further purified but was used directly in the next reaction. Although the pathway of the oxidation is not fully documented, it is possible to suggest a rational mechanism. It was observed that when the hydrolysis of the ester was carried out in the absence of oxygen, only the 2-hydroxyketone was formed and not the dienone. Subsequent reaction of this hydroxyketone with oxygen in basic solution gave the desired dienone. The mechanism proposed for this reaction is shown in Chart IV. The material (XLIII) obtained from the above oxidation was reacted with potassium t-butoxide in t-butyl alcohol according to the method of Baran (37) to form the enolate anion of the enol. This anion was then reacted with a large excess of methyl iodide to give the desired methoxydienone XLII as a white crystalline solid. It was found that XLII could be caused to undergo rearrangement with either a 2537 angstrom 7 watt source or a 450 watt source with emission maxima at both 2537 and 3600 angstroms. It was observed by ir that the disappearance of starting material was rapid during the first one to two hours of the reaction but decreased rather sharply as the reaction progressed. At the end of eight to ten hours in the case of the 7 watt source, or two to three hours in the case of the 450 watt source, the rate of disappearance of the starting material was so slow that further irradiation produced negligible



Chapter IV. Mechanism of Oxidation of 2-Hydroxyketones

results. Due to the fact that the enol ether function of the expected product would likely be acid labile, it was felt that the usual evaporative work up, which requires considerable contact with aqueous acid at temperatures in excess of 65°C, was too vigorous. For this reason the solvent was removed from the reaction mixture by lyophilization. It was found that this procedure was extremely satisfactory for removing aqueous acetic acid and that the time required to remove ca. 300 ml of solvent was only about four hours. Chromatography of the reaction product over silica gel gave 36 percent of the expected spiro hydroxy ketone XLIV as well as small amounts of mixtures of other compounds. While these additional compounds were not fully characterized, it was clear that XLIV was the major single compound formed in the reaction. Infrared analysis indicated that a small amount of a hydroazulene of the type LXVIII might be present in low yield but much less than had been observed in the case of XXXVI. Aside from recovered starting material, one additional compound was identified. This material was identical in spectral and physical properties to the 2-hydroxy dienone XLIII. In runs where adequate precautions were taken to insure the purity of the starting material, XLIII was, nonetheless, isolated in greater than trace amounts. The amount isolated from a given run seemed to be roughly related to the length of time of irradiation, larger amounts being obtained when the 7 watt source was used for extended periods of time. It is believed that this material arises from photochemical origins since allowing the reaction mixture to stand overnight at room temperature before solvent removal gave no significant increase in the amount of XLIII isolated. In one case the solvent was removed in the usual fashion (in vacuo evaporation on the steam

bath). Again no significant increase in the amount of XLIII was noted. The photochemical addition of protic solvents to double bonds is well documented (47a,b). Addition of water to the Δ^1 double bond of XLII would lead to structure LXIX. Loss of methanol from this structure would then give XLIII.

The 5,9-dimethyldienone, XLIX, was prepared from the octalone XLVII (See Chart V). Unlike octalone XXVII, XLVII could not be prepared in acceptable yield by condensing the appropriately substituted cyclohexanone with methyl vinyl ketone, but was prepared by an indirect approach. The difficulties of this reaction are discussed by Marshall (39) who also offers a synthesis of the compound. Recently, Caine and Tuller (48) also published a synthesis of this compound. Both methods are satisfactory for the preparation of XLVII, either giving yields of approximately 40 percent. Compound XLVII was transformed into XLIX via XLVI and in a manner analogous to that discussed above for the conversion of XXVII into XLII. The yields of the various steps, not unexpectedly, were similar to those reported for the steps leading to XLII. Irradiation of XLIX under conditions identical to those employed for XLII gave essentially identical results. The yield of spiroketone was 28 percent based on recovered starting material as compared to 35 percent for the monomethyl compound. The low yields in these reactions are somewhat disappointing. Possibly the use of methanol-acetic acid or glacial acetic acid would increase the amounts of spiroketones formed by prohibiting the formation of 2-hydroxy compounds. It is well accepted that the most stable stereochemical form of XLVII is that in which the 5-methyl group is in the α, equatorial configuration. Since this position

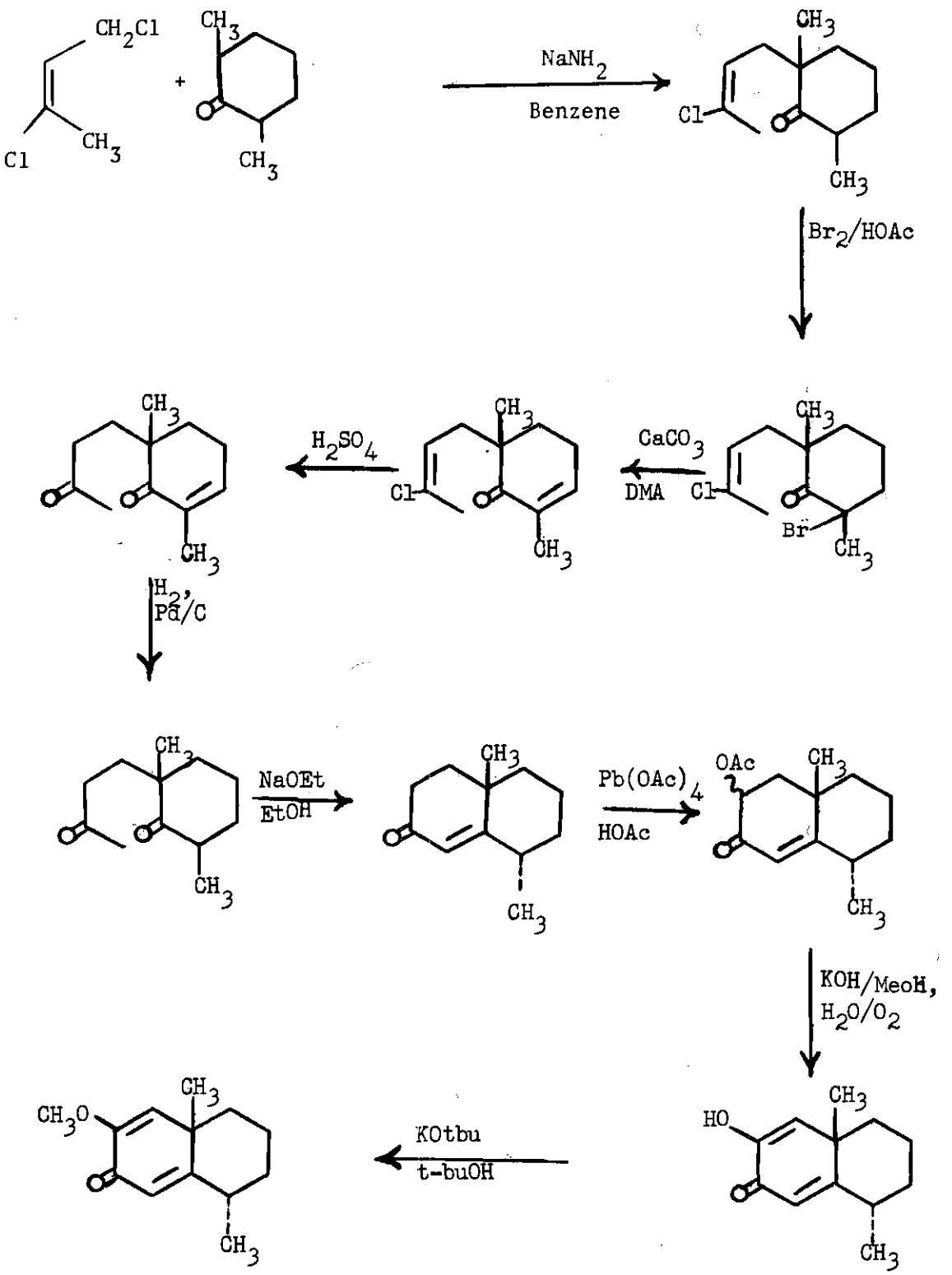


Chart V. Synthetic Route to 2-Methoxyoctalones.

is vinylogously activated, and since the compound is prepared under equilibrium conditions, it is felt that the material prepared during the course of this work was the 5α-methyl isomer. Indeed, no evidence to the contrary was found. In view of this fact, and considering the mechanism proposed for the photochemical rearrangement herein discussed, it follows that the relative stereochemistry of the spirohydroxyketone L, must be as shown. A sound knowledge of the stereochemistry of this compound is necessary to the work to be discussed hereafter.

As is mentioned in the paragraph above the stereochemistry of L is such that the 9-methyl group and 4-methylene group of the five membered ring may be considered trans to one another. Inspection of the structures of compounds belonging to the β-vetivone family reveal that if the C-3 carbonyl of L is to be used for the introduction of the three carbon side chain in molecules of this type, the relative stereochemistries of compounds produced in this fashion will be opposite to that found in the naturally occuring compounds. The remaining part of this discussion will detail the circumvention of this problem. Basically, the approach involves reduction of the C-3 carbonyl to methylene, hydrolysis of the remaining enol ether, and introduction of the three carbon side chain at the position of the new carbonyl function. The reason for study of the 2-methoxy dienones is then obvious, for such compounds not only have the appropriate functional groups for the desired influence on the rearrangement, but also provide a means to convert the rearranged product into an A-ring unsubstituted spirodecane of the proper stereochemistry for the synthesis of naturally occurring compounds related to β-vetivone.

The first approach was that of reduction of the C-3 carbonyl group with lithium aluminum hydride, preparation of the tosylate of the resulting alcohol, and lithium aluminum hydride reduction of the tosylate. Compound XLIV was chosen as a model system for these experiments. For obvious reasons, it seemed likely that any series of reactions applicable to XLIV would be equally applicable to L. Reduction of XLIV proceeded in the usual manner to give the desired alcohol. However, attempts to convert the alcohol to the tosylate with p-toluenesulfonyl chloride were unsuccessful. A successful method was devised and this will be discussed later.

A second attempt to remove the C-3 carbonyl involved Wolff-Kishner reduction of L. The Huang-Minlon modification of the reduction was employed according to a procedure communicated privately to the author by Professor Pierre Crabbe. Unfortunately, the material isolated from this reaction had no well-defined spectral properties.

The third possibility for removing the C-3 carbonyl was that of preparing the ethylene dithioketal of XLIV followed by desulfurization with Raney nickel in the usual manner. Reaction of the spiroketone with ethanedithiol in benzene containing a catalytic amount of boron trifluoride-etherate gave predominately the bis-dithioketal LXX. Only a small amount of the monodithioketal could be detected. Subsequent investigation of compound LXXI having the same keto-enol ether system by another worker in our laboratories (49) revealed that the reaction was not dependent on concentration, solvent, or reaction time, the bis-dithioketal being the major product regardless of conditions. One possible explanation of this observation lies in the fact that boron

trifluoride could form a complex with the oxygen of the enol ether which is then hydrolyzed by the water liberated on formation of the thioketal. At any rate, the reaction proved to be of no use to the proposed scheme.

A final approach involving hydroxy ketone starting materials involved the reduction of XLIV with palladium on carbon followed by further reduction with platinum oxide to give the diol LXXII. It was hoped that treatment of the material with a dehydrating agent such as thionyl chloride in pyridine would give rise to the desired enol ether LXXIII. Subsequent hydrolysis would then give the desired ketone LVII. Although the reduction appeared to proceed successfully to LXXII, dehydration gave only polymeric materials with no well defined spectral properties.

The remainder of the sequences attempted involved the dehydrated form of the hydroxy ketones. Both XLIV and L could be dehydrated successfully with thionyl chloride in pyridine and gave acceptable yields of the dehydro compounds LII and LIII, respectively. Dehydration of compound L was also attempted using phosphorous oxychloride. The reaction proceeded only partly to completion and gave an approximately 1:1 mixture of product and starting material, but in lower overall yield than when the reaction was carried out using thionyl chloride. Compound LIII was also subjected to the conditions of Wolff-Kishner reduction in an attempt to prepare compound LVI. Two procedures were employed. In the first, the semicarbazone of LIII was prepared and subjected to the conditions described by Cram (40) for the room temperature reduction in dimethyl sulfoxide. Spectral properties of the solid recovered were identical to those of the starting material. This same semicarbazone was

subjected to the conditions described earlier for the Wolff Kishner reduction of L. Only polymeric materials were obtained on workup. Compound LIII was also subjected to these conditions, but again to no avail as only dark intractable oils were obtained on work up.

The successful approach to the desired compounds (See Chart VI) was one involving reduction of the ketone LIII to its corresponding alcohol with lithium aluminum hydride followed by acetylation with acetic anhydride in pyridine, treatment with lithium in ethylamine, and hydrolysis. An attempt was made to reduce LIII with lithium aluminum hydride in the usual fashion. Work up of the reaction mixture gave, along with the desired alcohol, a large amount of a material whose infrared spectrum exhibited an absorption characteristic of a saturated cyclopentanone ring. Further investigation revealed that the normal mode of reduction was paralleled by 1,4-reduction of the cyclopentanone system to give rise to dihydro LIII in which the Δ 1 double bond had been reduced. Small amounts of the tetrahydro compound LXXIV were also detected. Reduction in an analogous fashion with sodium borohydride gave the same result with even larger amounts of the dihydro compound formed. It was felt, that the high concentration of reducing agent in the solution probably accounted for the undesirable course of the reduction. A standardized solution of lithium aluminum hydride in ether was prepared and an equivalent amount was added dropwise slowly to the stirred solution of LIII. Work up of the reaction gave an excellent yield of the desired compound LIV and no trace of the 1,4 reduction product obtained in the previous reaction was observed. Acetylation of LIV proceeded

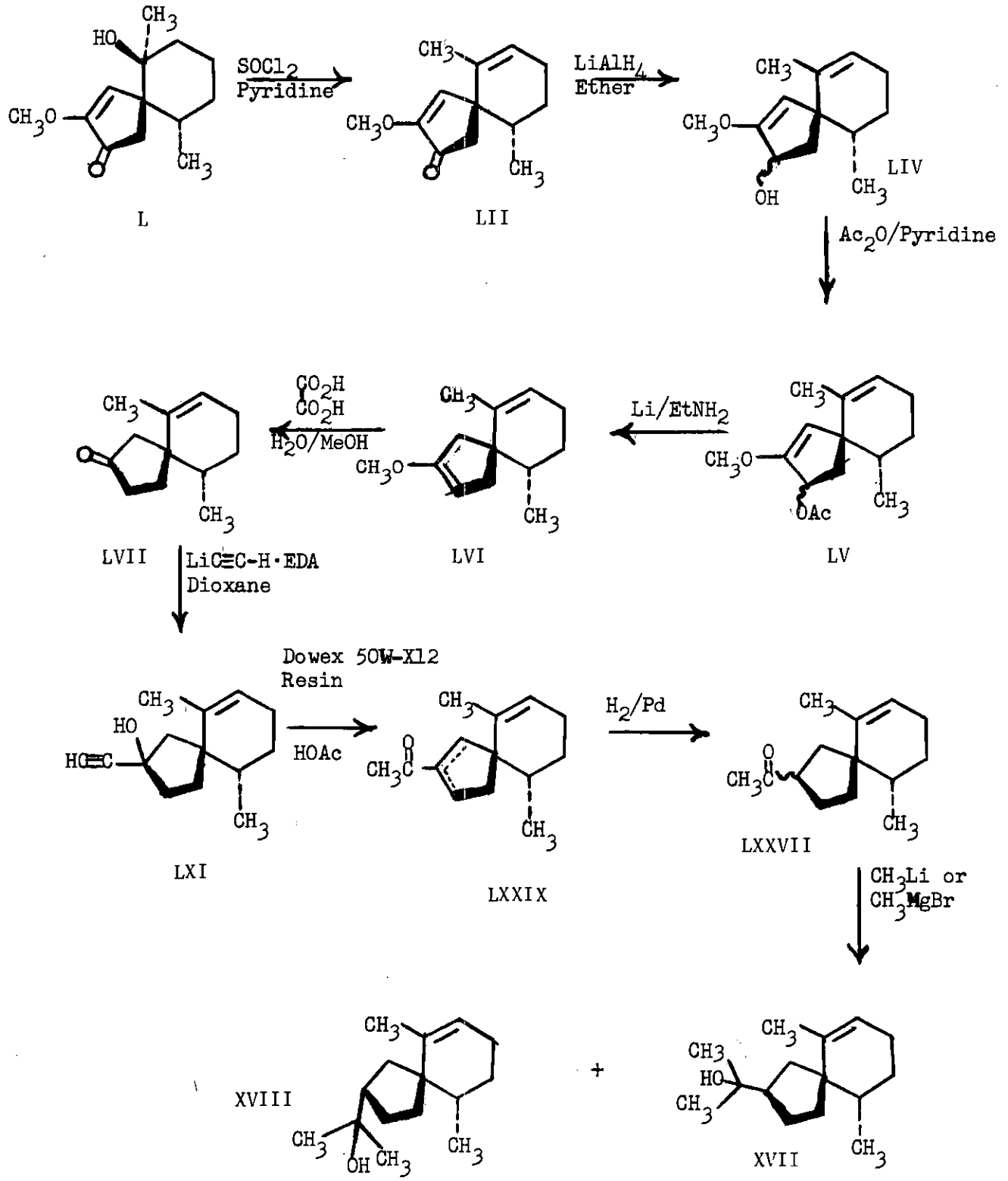


Chart VI. Synthetic Route to Hinesol and Agarospirol

smoothly to the acetate LV when a solution of LIV was stirred overnight at room temperature with acetic anhydride in pyridine.

The lithium-ethylamine reduction of LV was carried out in the manner of Henbest (41) in which the compound to be reduced is added dropwise to a solution of the required amount of lithium dissolved in dry ethylamine. Work up of this reaction mixture gave, not the desired compound LVI, but a complex mixture of compounds, the infrared spectrum of which indicated the presence of a saturated cyclopentanone system. In view of the nature of the reaction and the past history of the sample it was believed that such an absorption could only arise from a compound of the type LVII. Also, the nmr spectrum of the reaction mixture was notable in the near absence of an absorption corresponding to that expected for a methoxyl group. Considering the success of the inverse lithium aluminum hydride reduction carried out on LIII, it seemed likely that this procedure might be suitable for reduction of the acetateLV with lithium in ethylamine. In fact, when a solution of lithium wire dissolved in dry ethylamine was added dropwise to a solution of LV in dry ethylamine, the reaction gave an excellent yield of the desired compound, LVI. It was observed, however, that if addition of the lithium solution was continued to the point that the blue color persisted for more than a few seconds, the yield of LVI was significantly reduced. It was also noted that if the dropwise addition of the reducing agent was extended over a long period of time, varying amounts of LIV were also obtained. The exact amount depended to a large extent on the length of time during which the addition was carried out. It is not understood what secondary reaction takes place in the presence of excess lithium,

except that the product or products are not enol ethers. It is probable this secondary reaction is the same reaction that takes place when the reduction is conducted in the normal fashion, which suggests, in fact, that the loss of acetate is the first reaction to take place. This is followed by interaction of the enol ether system with the reducing agent in some fashion. The formation of LIV is best explained by considering the fact that, as the reduction proceeds, the concentration of lithium ethylamide is increased. This may, in turn, attack unreacted molecules of the acetate to give cleavage of the ester to the parent alcohol. Thus, the observation that short reaction times are consistent with the best yields of LVI. The initial disappearance of the blue color of the lithium ethylamine solution is extremely rapid, and, if the reaction is quenched immediately when the uptake of this color decreases, the yields of LVI are not altered which indicates that the reduction is extremely rapid with respect to competing reactions in the absence of a large excess of reducing agent. Hydrolysis of LVI was accomplished simply by stirring the compound with a solution of aqueous methanolic oxalic acid at room temperature for 0.5 hr.

Another approach for converting LV to LVII was considered prior to the work using lithium in ethyl amine. This involved the hydrolysis of LV to the ketone, LXXV. It was thought that LXXV should react readily with lithium in liquid ammonia to give the ketone LVII. Unfortunately, all attempts to hydrolyze the material resulted in either recovery of unchanged starting material or in material in which both the acetate and enol ether functions had been removed. Indeed, experiments conducted on the model system LXXI indicated that in such systems, the

acetate was the first group to undergo hydrolysis. Presumably this was due to the strong electron withdrawing effect exerted on the enol ether system by the acetate group for, as described above, the same system in the absence of the acetate group is readily hydrolyzable under mild conditions.

The spiroketone prepared from L was compared with the corresponding stereoisomeric ketone LX prepared from LIX and LVIII according to the methods of Kropp (43) and Marshall (20) described in the experimental section. Although the infrared spectra of the two compounds were almost identical, the nmr spectra were sufficiently different to confirm that the two compounds were not identical. The AB quartet for the C-4 proton absorptions of LX was clearly distinguishable at 2.10 and 2.24 ppm with a coupling constant of -19 Hz (see plate 2) while for LVIII, an absorption was observed at approximately 2 ppm which on first inspection appeared to be a sharp singlet. Further investigation of the nmr spectrum using a 100 MHz instrument revealed that the peak was in reality a doublet which composed the inner pair of peaks of an AB quartet at 2.15 and 2.16 ppm. This splitting of the apparent singlet was also observable in the expanded spectrum of a 60 MHz determination. J_{AB} was again observed to be -19 Hz (See plate 1). It was felt that the most promising approach to the methyl ketone LXXVII was the addition of sodium or lithium acetylide to the carbonyl group LVII followed by conversion of the resulting acetylene to the ketone LXXIX. Since LXXVII had been previously converted to an isomeric mixture of dl-hinesol and dl-agarospirol, this would complete the synthesis of these two compounds.

Attempts to react LVII with both sodium and lithium acetylide were unsuccessful, and gave only unreacted starting material on work up. Since Huffman (44) had successfully reacted compounds of a similar type with lithium acetylide-ethylenediamine complex, this method was also attempted. The infrared spectrum of the product showed an absorption corresponding to an acetylenic C-H stretch at 3300 cm^{-1}, although the nmr and mass spectral data were not entirely consistent with the structure LXI. Since Huffman (44) had been successful in converting acetylenic carbanols to unsaturated methyl ketones in good yield using Dowex 50-W X-12 ion exchange resin (H+ phase), this method was employed on the crude reaction product obtained on treatment of LVII with the lithium acetylide reagent. The products of this reaction were examined by glc and were shown to be a mixture of several different compounds consisting of approximately 40-50 percent of a single component. This component was isolated by preparative glc and shown not to be the desired methyl ketone LXXIX but to be identical to the octalone XLVII. An explanation of these facts was found in the proposal that the acetylenic absorption observed in the product of reaction of LVII was spurious, and that, in reality, the major component of the initial mixture was in fact the unreacted ketone LVII. It was further proposed that this ketone, on subsequent exposure to the reaction conditions prescribed by Huffman (44), underwent an acid catalyzed rearrangement to give XLVII. This proposed rearrangement is shown in scheme VII. To verify the possibility of such a rearrangement the spiroketone LVII was subjected to the conditions mentioned above for the conversion of acetylenic carbanols to methyl ketones. Indeed, work up of the reaction mixture

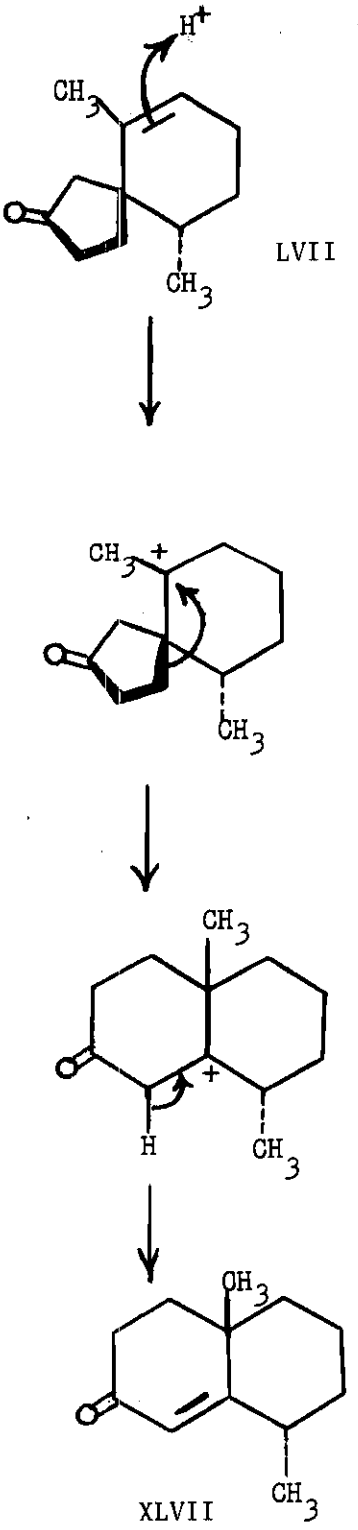


Chart VII. Mechanism of Acid Catalyzed Rearrangement of LVII.

gave an oil the major component of which showed spectral properties identical to those of XLVII and to the material obtained on attempted hydration of crude LXI.

CHAPTER V

CONCLUSIONS

Two additional compounds in the series of cross-conjugated cyclohexadienones containing electron withdrawing substituents on the dienone chromophore were synthesized and irradiated. The results of these irradiations are consistent with previously reported results in similar systems and fully support the proposed mechanism for such rearrangements.

One new compound in the series of cross-conjugated cyclohexadienones containing electron donating groups on the dienone chromophore was prepared and irradiated. In addition to supporting the proposed mechanism and exhibiting analogous behavior to such compounds already studied, the successful isolation of a spirohydroxyketone product from this rearrangement opened a new and facile route to spirodecane structures having a relative stereochemistry which would be of interest in the synthesis of compounds related to β-vetivone.

A successful synthetic pathway was devised for converting the spirohydroxyketone formed in the rearrangement mentioned above into the spiroketone LVII. This compound should be invaluable in the synthesis of a number of natural products having spirodecane structures. This compound, along with the previously reported stereoisomeric spiroketone LX allows the preparation of A-ring substituted spirodecanes which, in effect, may have either of the two possible stereochemical fusions at the spiro center by simply choosing the appropriate ketone LX or LVII.

In addition to the successful preparation of LVII, the information obtained on further attempts to convert LVII to hinesol and agarospirol indicate that the conversion is quite feasible, and these findings should prove of value to others who may attempt the conversion.

Also, the findings concerning the reactivity of systems containing α-methoxy-α,β-unsaturated ketones toward chemical reducing agents should be of aid to those interested in these systems for synthetic purposes. It is noteworthy that in almost all reactions that were unsuccessful in this system, there was a definite loss of the enol ether portion of the molecule as determined by nmr examination. This should serve as valid proof of the extreme reactivity of this system.

Finally the rearrangement of spiro systems of the type LVII in acid media to give naphthalenoid type ring systems was discovered, and may be of interest in connection with biosynthetic pathways.

CHAPTER VI

RECOMMENDATIONS

Further attempts to prepare the 4-carboxy derivative LXXX and the 4-carbomethoxy derivative XXVIII should be made and the irradiation of these compounds should be studied. The 4-methoxy compound LXXXI (49) should be investigated with respect to its ability to undergo rearrangement. The irradiations of the 2-methoxy and 4-cyano derivatives (XLIX, XLII and XXXVI, respectively) should be studied with respect to the minor products formed in the reaction. The 4-cyano spiroketone should be studied further as to possibilities to convert the cyano group into other functional groups which might be of use in synthetic work.

The reaction of ethanedithiol with systems of the type XLIX should be fully investigated. Since 4-methoxyoctalone systems are readily available synthetically (50) a reaction of the type attempted in the work under discussion would be useful in preparing 5-substituted-4-keto-octalones. The mechanism of hydrolysis of the 2-methoxyl group during such dithio ketalizations should be considered in detail.

The reaction of lithium aluminum hydride with allylic ketones bearing 2-methoxyl substituents should be studied both as to the mode of reduction and as to the mechanism by which the 2-substituent is lost.

The reduction of systems of the type mentioned above with lithium in ammonia and lithium in ethylamine should be investigated with respect to the apparent hydrolysis of the enol ether function. The nature of the requirement for inverse addition of the reducing agent should also be investigated.

Finally, other methods for the conversion of LVII into LXXIX should be sought and attempted. The reaction of LVII with Dowex 50W-X12 (H^+ phase) should also be investigated as well as the reaction of other similar systems with the resin and with other acid catalysts to determine the generality of the rearrangement and specificity of the catalyst.

LITERATURE CITED*

1. H. Kahler, Arch. Pharm., 34, 318(1830).

2. O. L. Chapman, ed. "Organic Photochemistry", 1. Marcel Dekker, Inc. New York, 1967.

3. H. E. Zimmerman and D. I. Schuster, J. Am. Chem. Soc., 84, 4527 (1962).

4. O. L. Chapman in W. A. Noyes, Jr., G. S. Hammond, and J. N. Pitts, Jr., eds. "Advances in Photochemistry", 1. Wiley-Interscience, New York (1963).

5. G. A. Taylor, Chem. Comm., 896 (1967).

6. P. J. Kropp and W. F. Erman, J. Am. Chem. Soc., 85, 2456(1963).

7. P. J. Kropp, J. Am. Chem. Soc., 86, 4053(1964).

8. D. Caine and J. B. Dawson, J. Org. Chem., 29, 3108(1964).

9. D. Caine, J. F. Debardeleben, Jr., and J. B. Dawson, Tetrahedron Letters, p 3627 (1966).

10. J. F. Debardeleben, Jr., Ph.D. Thesis, Georgia Institute of Technology, Atlanta, Georgia, 1967.

11. D. Caine and J. F. Debardeleben, Jr., Tetrahedron Letters, 4585 (1965).

12a. T. Nozoe and S. Ito, "Progress in the Chemistry of Natural Products", Vol. XIX, Springer-Verlag, Vienna(1961).
b. P. deMayo, "Mono and Sesquiterpenoids", Interscience Publishers Inc., New York(1959).
c. W. Herz, Abstracts of the 19th National Organic Symposium of the American Chemical Society, June 13-17, p. 67, 1965, Tempie, Arizona.

13. D. H. R. Barton, J. T. Pinhey, and R. J. Wells, J. Chem. Soc., 2518(1964).

*For the complete title of all journals referred to, see Chemical Abstracts, Vol. 55, p, 1J(1961), and supplements thereafter.

14. R. B. Bates and R. C. Seagel, J. Am. Chem. Soc., 84, 1307 (1962).

15a. G. Buchi and H. J. E. Loewenthal, Proc. Chem. Soc., 280(1962).
b. G. Buchi, J. M. Kaufman, and H. J. E. Loewenthal, J. Am. Chem. Soc., 88, 3403(1966).

16. G. Buchi, J. W. Chow, T. Matsuura, and T. L. Popper, Tetrahedron Letters No. 6, 14(1959).
L. Dolejs and F. Sorm, ibid., No. 10, 1(1959).

17. M. Palmade, R. Pesnelle, J. Streith, and G. Ourisson, Bull. Soc. Chem. France, 1950(1963).
R. Pesnelle and G. Ourisson, J. Org. Chem., 30, 1744(1965).

18. A. St. Pfau and Pl. A. Plattner, Helv. Chim. Acta., 23, 768(1940).
Y. R. Naves and R. Perottet, ibid., 24, 243(1941).

19. W. Z. Chow, O. Motl, and F. Sorm, Coll. Czech. Chem. Comm. 27, 1962(1914).

20. J. A. Marshall and P. C. Johnson, J. Am. Chem. Soc., 89, 2750 (1967).

21. K. Endo and P. deMayo, Chem. Commun., 89(1967).

22. K. R. Varma, M. C. Maheshwari, and S. C. Battagharyya, Tetrahedron, 21, 115(1965).

23. I. Yoshioka and T. Kimura, Chem. Pharm. Bull. (Tokyo), 13(12), 1430(1965).

24. D. Henneberg and K. Casper, Chemical Formulae From Mass Determination, Distributed by Fried. Krupp, Mess-und-Analysentechnik, Breman, Germany.

25. W. S. Johnson and W. P. Schneider, Org. Syn., Coll. Vol. IV, 132(1963).

26. I. C. Nigam and L. Levi, Can. J. Chem., 40, 2083(1962).

27. E. Wenkert and G. Jackson, J. Am. Chem. Soc., 81, 5601(1959).

28a. N. C. Ross and R. Levine, J. Org. Chem., 29, 2341(1964).
b. Prepared according to the proc. outlined in Org. Syn., Coll. Vol. II, pp. 165.

29. D. Burn, D. N. Kirk, and V. Petrow, Proc. Chem. Soc., 14(1960).

30. R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler, and W. M. McLamore, J. Am. Chem. Soc., 74, 4223(1952).

31. C. Djerassi and D. Marshall, J. Am. Chem. Soc., 80, 3986(1958).

32. M. E. Kuehne, J. Am. Chem. Soc., 83, 1492(1961).

33. H. M. Kissman, A. M. Hoffman, and M. J. Weiss, U. S. Patent No. 3,035,051(to American Cyanamid Co.)May 15, 1962.

34. S. Soloway and S. H. Wilen, Anal. Chem., 24, 979(1952).

35. E. Seeback and T. Reichstein, Helv. Chim. Acta., 27, 948(1944).

36. P. N. Rao and L. D. Axelrod, J. Am. Chem. Soc., 82, 2830(1960).

37. J. S. Baran, J. Am. Chem. Soc., 80, 1687(1958).

38. W. J. Powers, III, Ph.D. Thesis, Georgia Institute of Technology, Atlanta, Georgia, 1968.

39. J. A. Marshall and D. J. Schaeffer, J. Org. Chem., 30, 3642(1965).

40. D. J. Cram, M. R. V. Sahyan, and G. R. Knox, J. Am. Chem. Soc., 84, 1734(1962).

41. A. S. Hallsworth, H. B. Henbest, and T. L. Wrigley, J. Chem. Soc., 1969(1957).

42. Incorrectly reported by Marshall (ref. 20) as being prepared by Kropp (ref. 6).

43. P. J. Kropp, J. Am. Chem. Soc., 87, 3914 (1965).

44. J. W. Huffman and P. G. Arapakos, J. Org. Chem., 30, 1604(1965).

45. J. F. Debardeleben, Jr., Private communication.

46. H. B. Henbest, D. N. Jones, and G. P. Slater, J. Chem. Soc., 4472(1961).

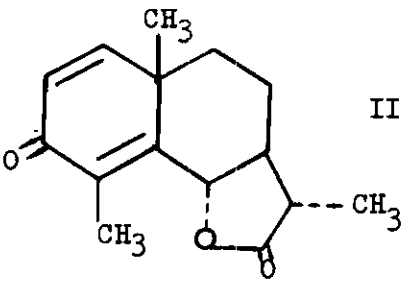
47a. J. A. Marshall, Accts. of Chem. Research, 2, 33(1969).
b. T. N. Hucherby, N. A. J. Rogers, and A. Satiar, Tetrahedron Letters, 1113(1967).

48. D. Caine and F. N. Tuller, J. Org. Chem., 34, 222(1969).

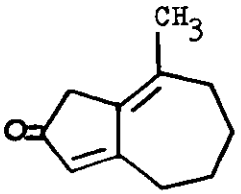
49. P. F. Ingwalson, Unpublished work, Georgia Institute of Technology, Atlanta, Georgia.

50. E. Wenkert and D. A. Berges, J. Am. Chem. Soc., 89, 2507(1967).

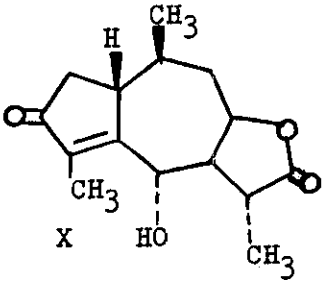
APPENDIX



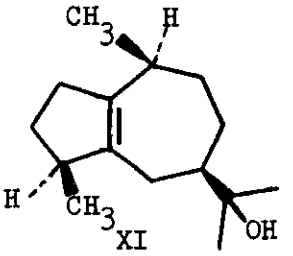
II



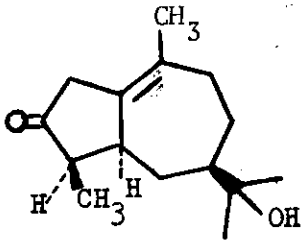
IX



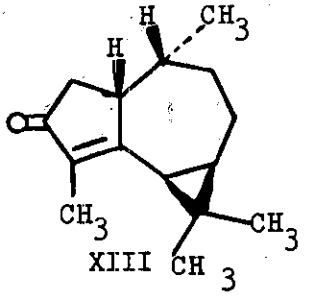
X



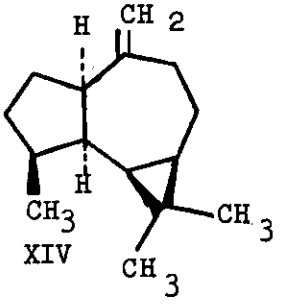
XI



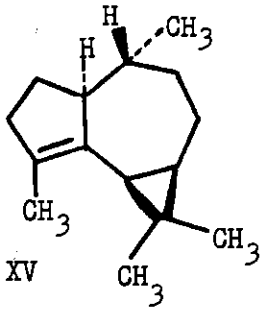
XII



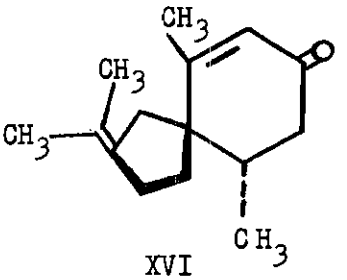
XIII



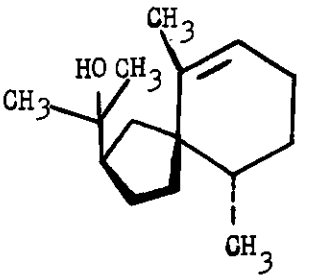
XIV



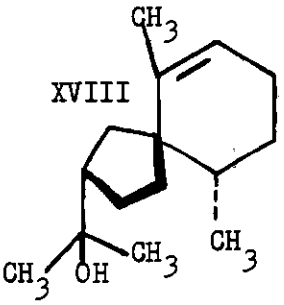
XV



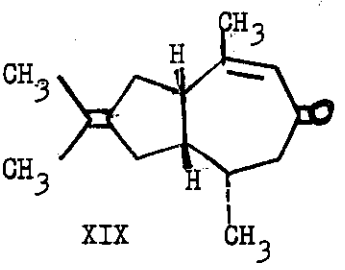
XVI



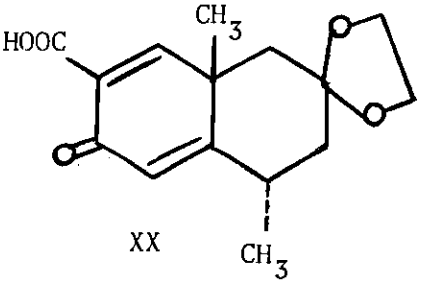
XVII



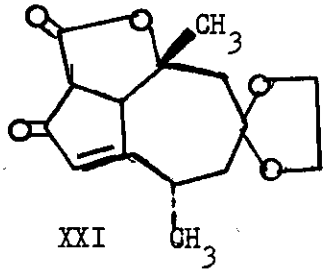
XVIII



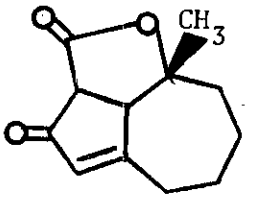
XIX



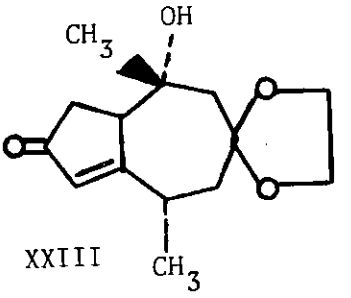
XX



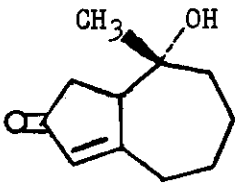
XXI



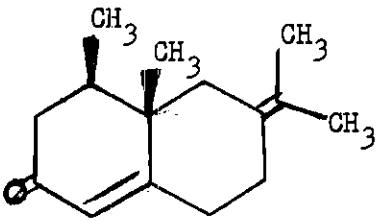
XXII



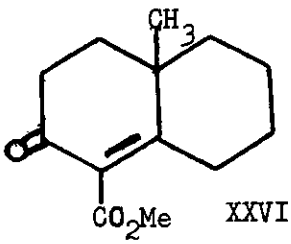
XXIII



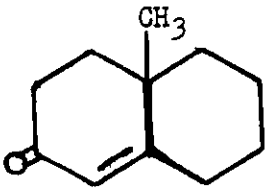
XXIV



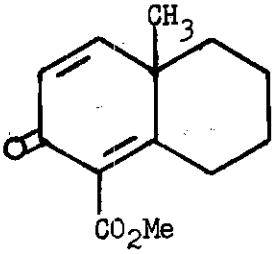
XXV



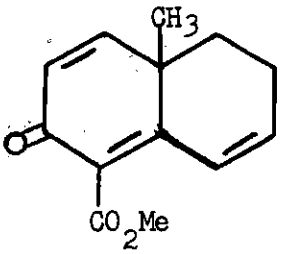
XXVI



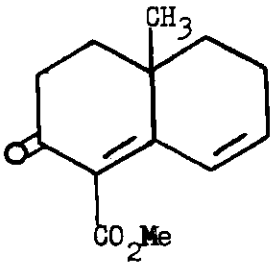
XXVII



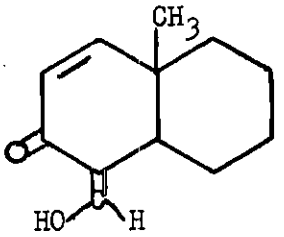
XXVIII



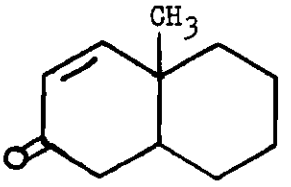
XXIX



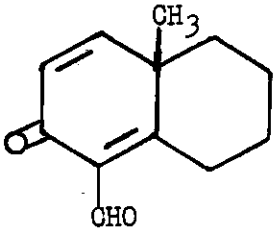
XXX



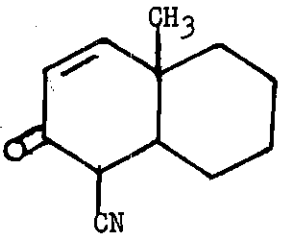
XXXI



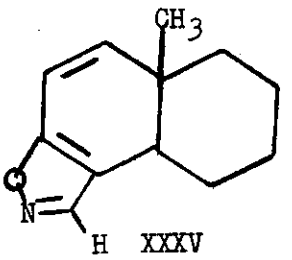
XXXII



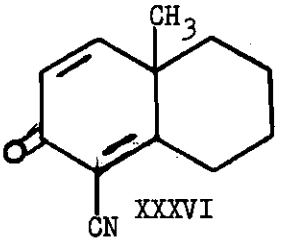
XXXIII



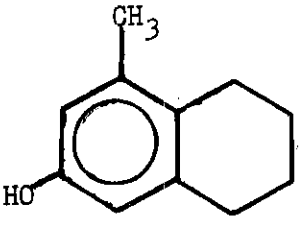
XXXIV



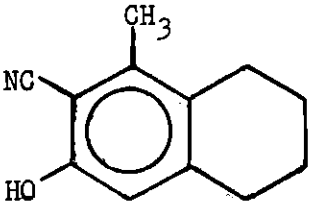
XXXV



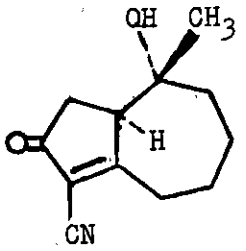
XXXVI



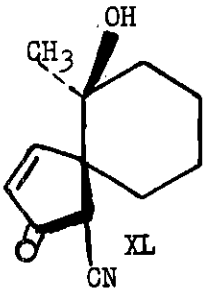
XXXVII



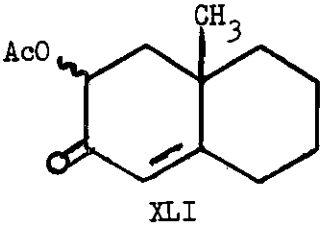
XXXVIII



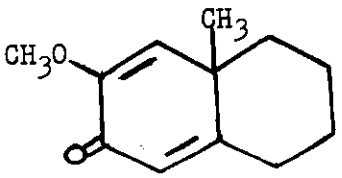
XXXIX



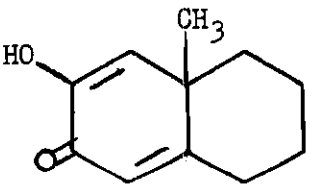
XL



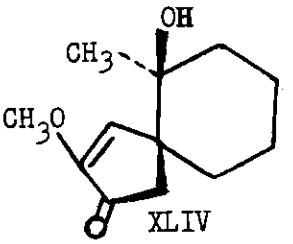
XLI



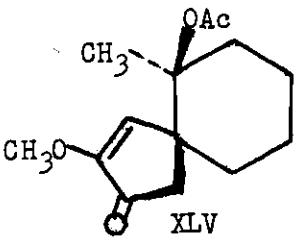
XLII



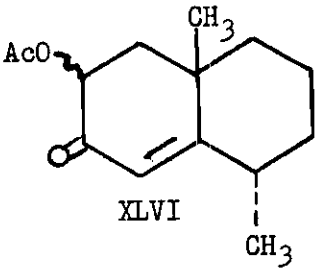
XLIII



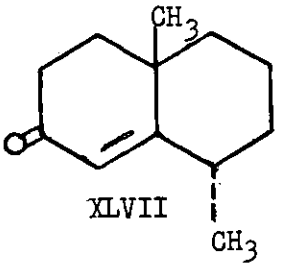
XLIV



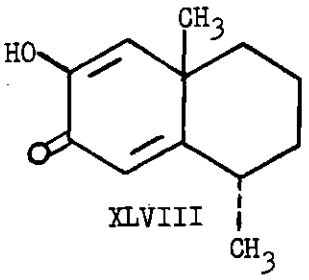
XLV



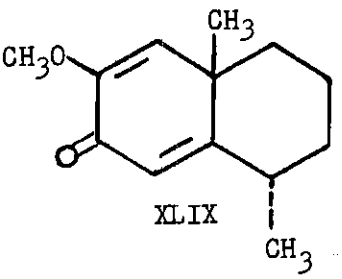
XLVI



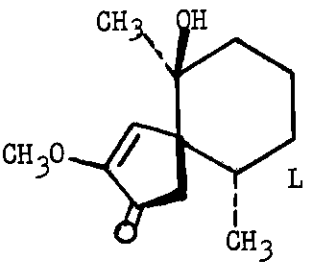
XLVII

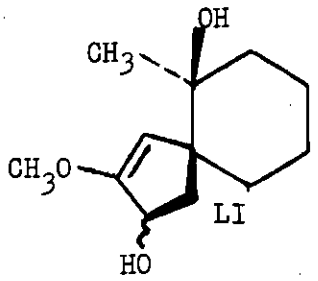


XLVIII

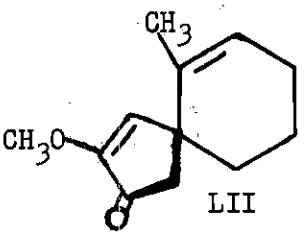


XLIX

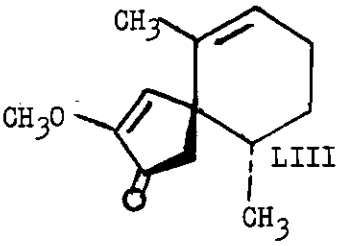




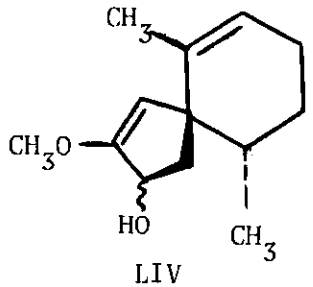
LI



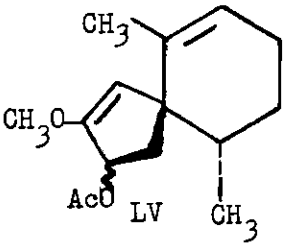
LII



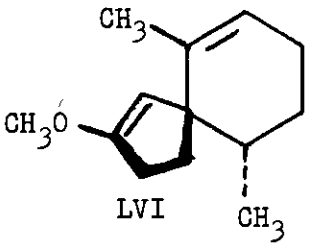
LIII



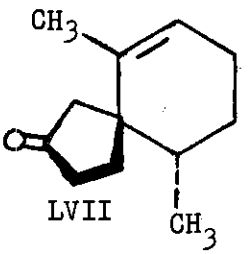
LIV



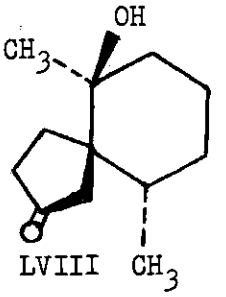
LV



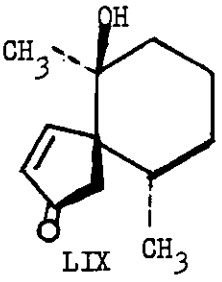
LVI



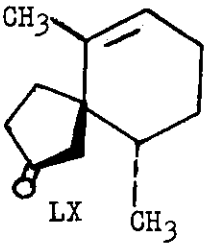
LVII



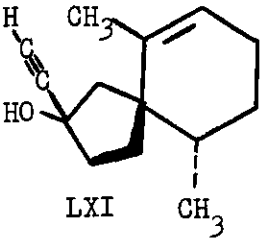
LVIII



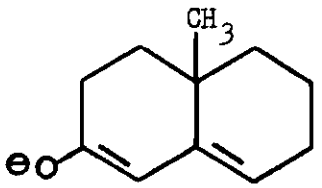
LIX



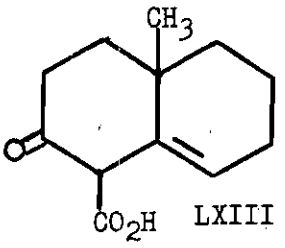
LX



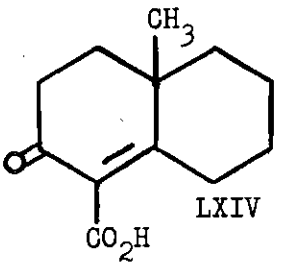
LXI



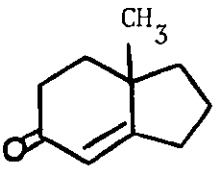
LXII



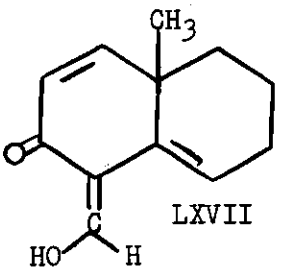
LXIII



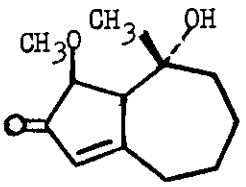
LXIV



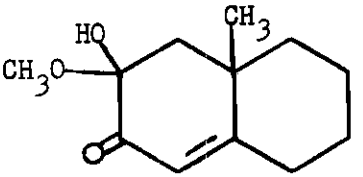
LXVI



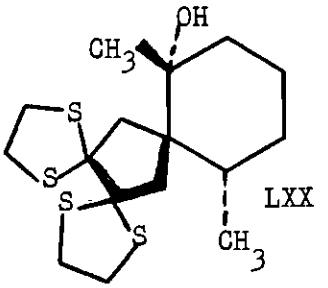
LXVII



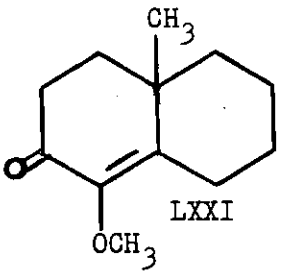
LXVIII



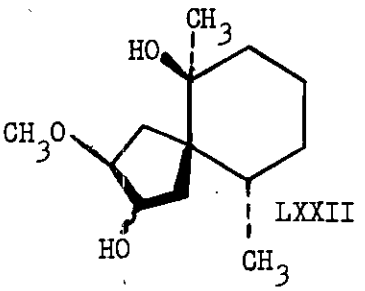
LXIX



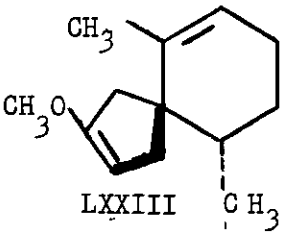
LXX



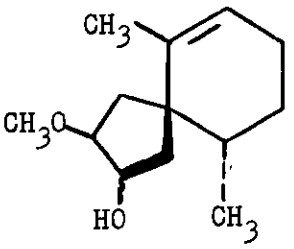
LXXI



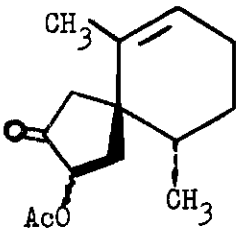
LXXII



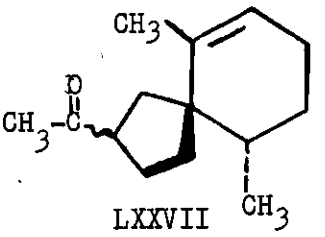
LXXIII



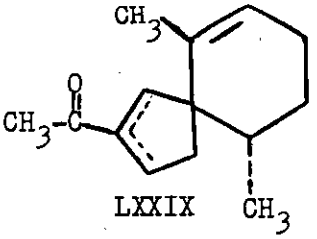
LXXIV



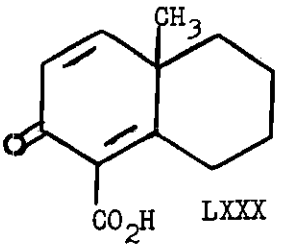
LXXV



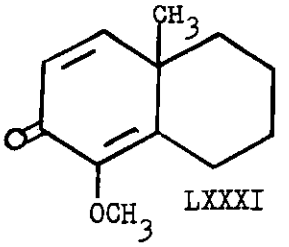
LXXVII



LXXIX



LXXX



LXXXI

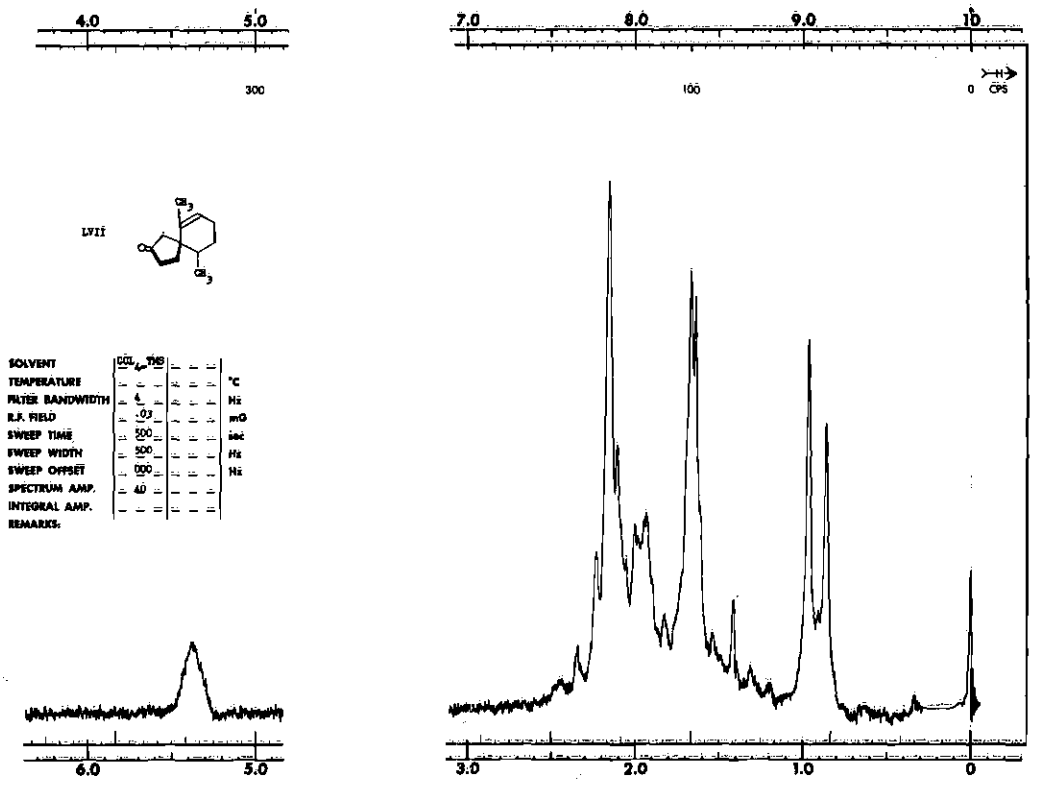


Plate 1-Nuclear magnetic resonance spectrum of LVII

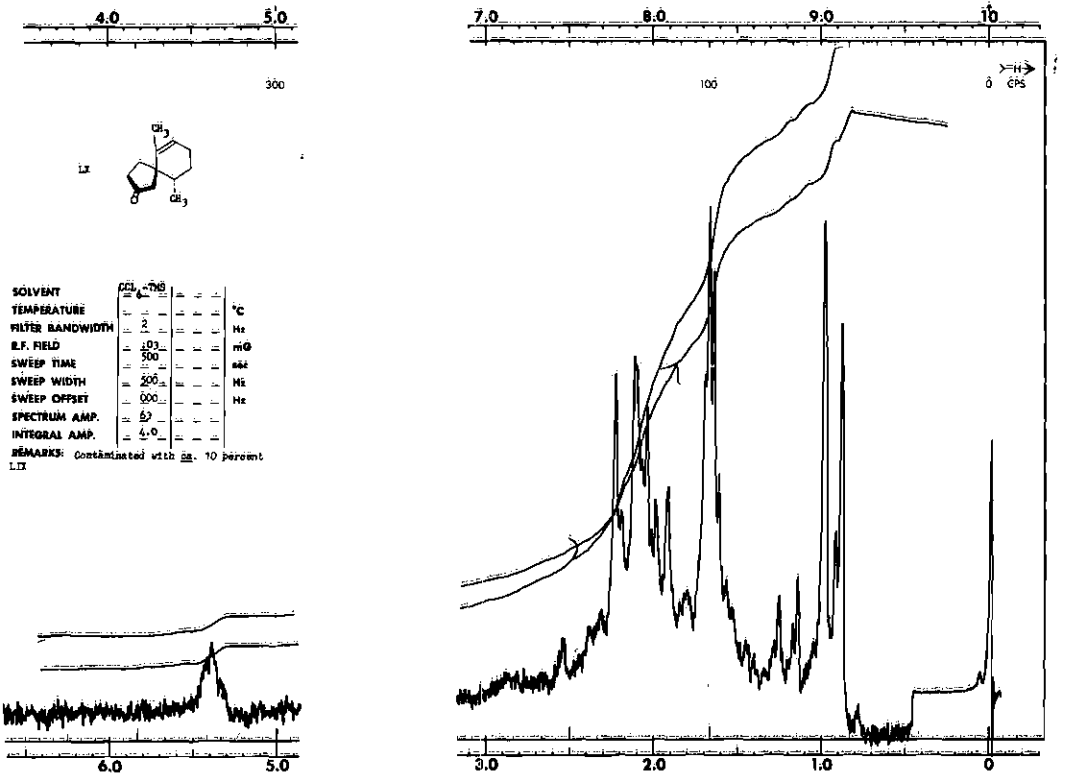


Plate 2-Nuclear magnetic resonance spectrum of LX

VITA

James Byron Dawson, son of Mr. and Mrs. J. L. Dawson, was born in Athens, Georgia, on November 22, 1941.

He attended elementary and secondary schools in Winterville, Georgia, and was graduated from Athens High School, Athens, Georgia in 1960. He received the Bachelor of Science Degree in Chemistry from the Georgia Institute of Technology in 1965. He began graduate work at the Georgia Institute of Technology in April, 1965, where he was awarded a National Defense Education Act, Title IV, predoctoral fellowship. Upon completing his graduate study he will be employed as assistant director of the Georgia Crime Laboratory.

He is a member of the American Chemical Society, The Chemical Society(London), and an associate member of the Society of the Sigma Xi.

He is married to the former Carole Agnes Burroughs and has two children, Lisa Carole, and Charles Byron.